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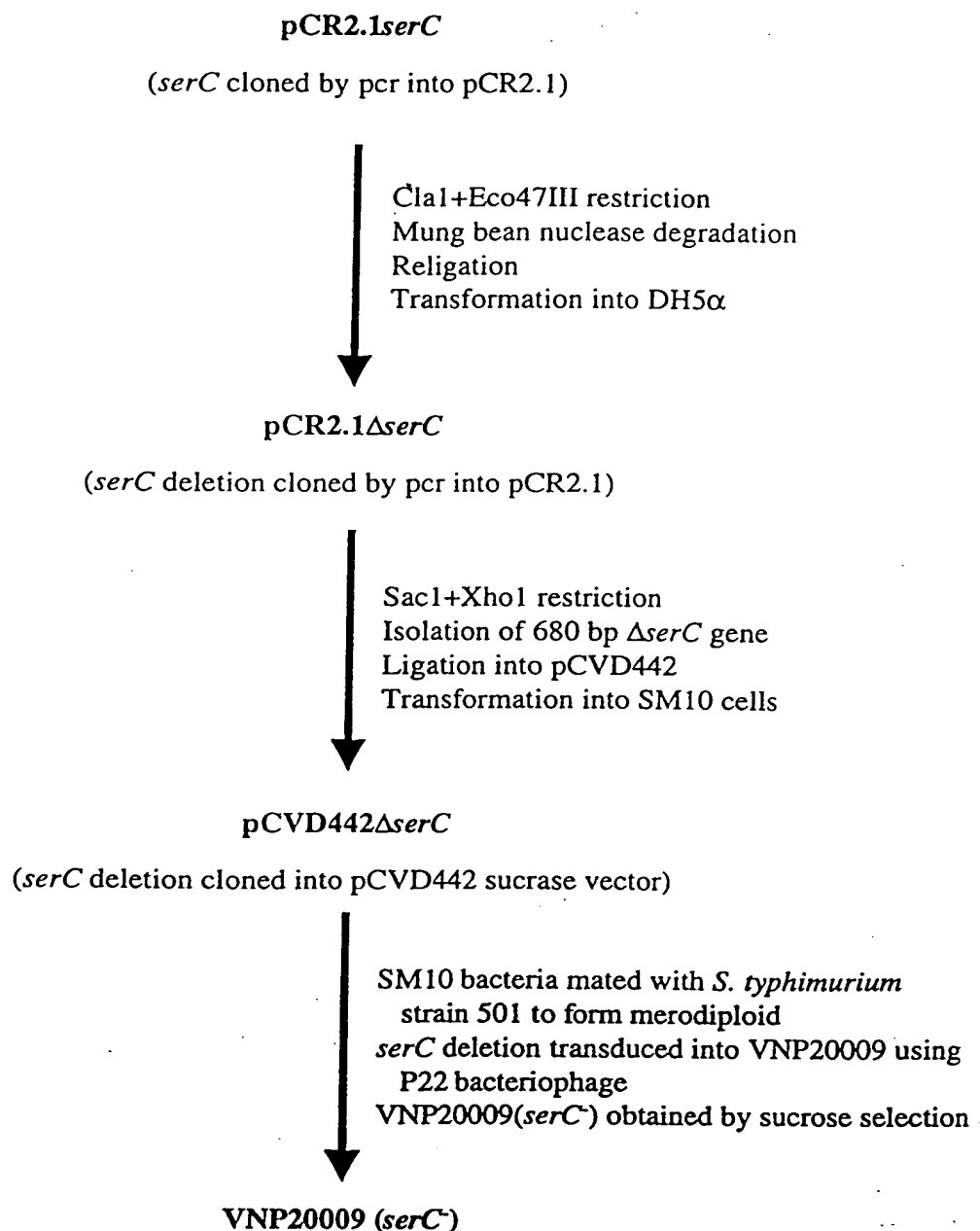
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M	V	R	S	S	S	R	T	P	S	D	K	P	V	A
CAT	GTA	GTT	GCT	AAC	CCT	CAG	GCA	GAA	GGT	CAG	CTG	CAG	TGG	CTG
H	V	V	A	N	P	Q	A	E	G	Q	L	Q	W	L
AAC	CGT	CGC	GCT	AAC	GCC	CTG	CTG	GCA	AAC	GGC	GTT	GAG	CTC	CGT
N	R	R	A	N	A	L	L	A	N	G	V	E	L	R
GAT	AAC	CAG	CTC	GTG	GTA	CCT	TCT	GAA	GGT	CTG	TAC	CTG	ATC	TAT
D	N	Q	L	V	V	P	S	E	G	L	Y	L	I	Y
TCT	CAA	GTA	CTG	TTC	AAG	GGT	CAG	GGC	TGC	CCG	TCG	ACT	CAT	GTT
S	Q	V	L	F	K	G	Q	G	C	P	S	T	H	V
CTG	CTG	ACT	CAC	ACC	ATC	AGC	CGT	ATT	GCT	GTA	TCT	TAC	CAG	ACC
L	L	T	H	T	I	S	R	I	A	V	S	Y	Q	T
AAA	GTT	AAC	CTG	CTG	AGC	GCT	ATC	AAG	TCT	CCG	TGC	CAG	CGT	GAA
K	V	N	L	L	S	A	I	K	S	P	C	Q	R	E
ACT	CCC	GAG	GGT	GCA	GAA	GCG	AAA	CCA	TGG	TAT	GAA	CCG	ATC	TAC
T	P	E	G	A	E	A	K	P	W	Y	E	P	I	Y
CTG	GGT	GGC	GTA	TTT	CAA	CTG	GAG	AAA	GGT	GAC	CGT	CTG	TCC	GCA
L	G	G	V	F	Q	L	E	K	G	D	R	L	S	A
GAA	ATC	AAC	CGT	CCT	GAC	TAT	CTA	GAT	TTC	GCT	GAA	TCT	GGC	CAG
E	I	N	R	P	D	Y	L	D	F	A	E	S	G	Q
GTG	TAC	TTC	GGT	ATT	ATC	GCA	CTG	TAA						
V	Y	F	G	I	I	A	L	*						

FIG. 1

Derivation of the VNP20009(*serC*⁻) strain.**FIG. 2**

Quantitation of TNF α expression by pTS-BrpTNF α Clone 2.

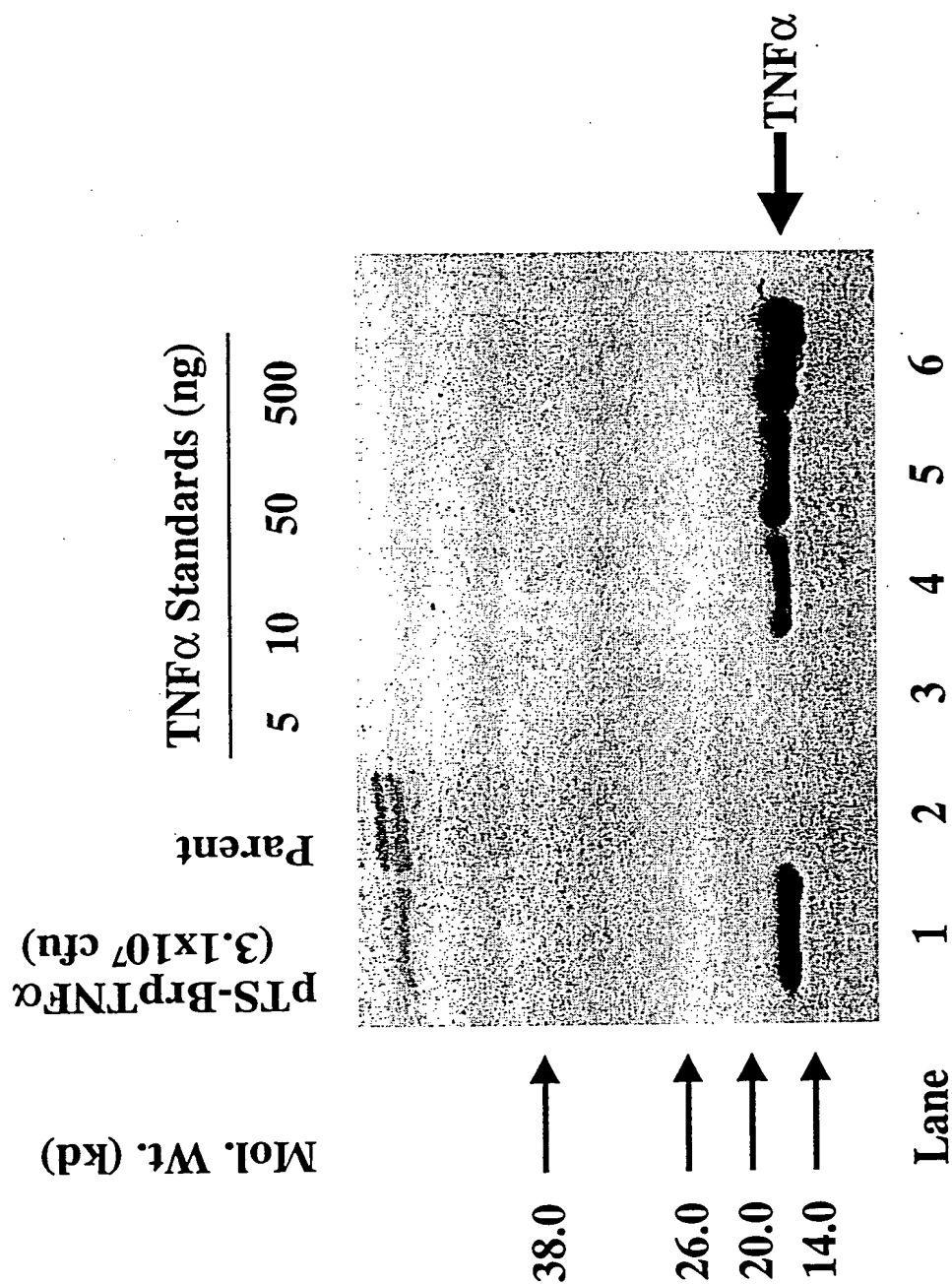


FIG. 3

ATG AAA AAG ACA GCT ATC GCG ATT GCA GTG GCA CTG GCT GGT TTC
 M K K T A I A I A V A L A G F
 GCT ACC GTA GCG CAG GCC CAT ATG GTA CGT AGC TCC TCT CGC ACT
 A T V A Q A H M V R S S S R T
 CCG TCC GAT AAG CCG GTT GCT CAT GTA GTT GCT AAC CCT CAG GCA
 P S D K P V A H V V A N P Q A
 GAA GGT CAG CTG CAG TGG CTG AAC CGT CGC GCT AAC GCC CTG CTG
 E G Q L Q W L N R R A N A L L
 GCA AAC GGC GTT GAG CTC CGT GAT AAC CAG CTC GTG GTA CCT TCT
 A N G V E L R D N Q L V V P S
 GAA GGT CTG TAC CTG ATC TAT TCT CAA GTA CTG TTC AAG GGT CAG
 E G L Y L I Y S Q V L F K G Q
 GGC TGC CCG TCG ACT CAT GTT CTG CTG ACT CAC ACC ATC AGC CGT
 G C P S T H V L L T H T I S R
 ATT GCT GTA TCT TAC CAG ACC AAA GTT AAC CTG CTG AGC GCT ATC
 I A V S Y Q T K V N L L S A I
 AAG TCT CCG TGC CAG CGT GAA ACT CCC GAG GGT GCA GAA GCG AAA
 K S P C Q R E T P E G A E A K
 CCA TGG TAT GAA CCG ATC TAC CTG GGT GGC GTA TTT CAA CTG GAG
 P W Y E P I Y L G G V F Q L E
 AAA GGT GAC CGT CTG TCC GCA GAA ATC AAC CGT CCT GAC TAT CTA
 K G D R L S A E I N R P D Y L
 GAT TTC GCT GAA TCT GGC CAG GTG TAC TTC GGT ATT ATC GCA CTG
 D F A E S G Q V Y F G I I A L
 TAA
 *

FIG. 4

Expression and processing of a *trc* promoter-driven *ompA*-TRAIL fusion gene product in JM109 bacteria.

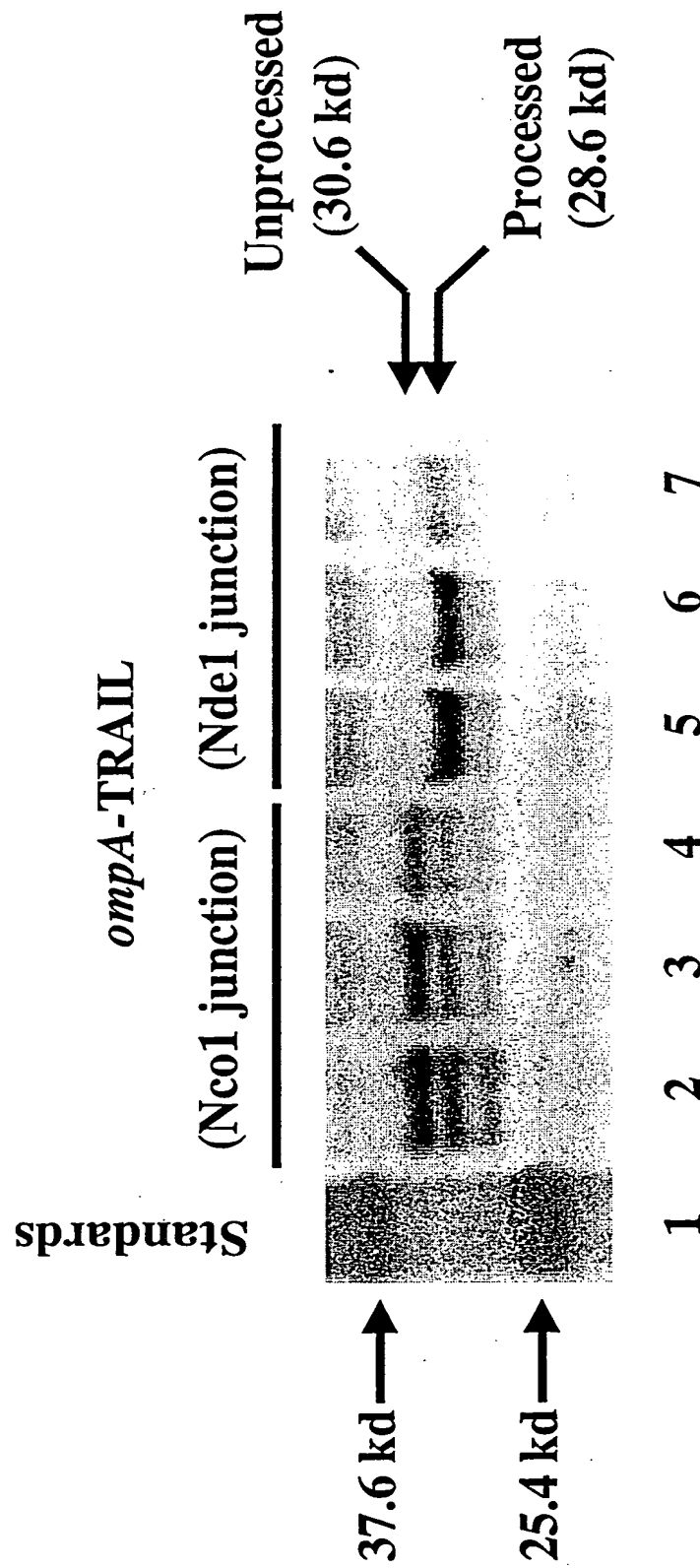


FIG. 5

ATG AAA AAG ACA GCT ATC GCG ATT GCA GTG GCA CTG GCT GGT TTC
 M K K T A I A I A V A L A G F
 GCT ACC GTA GCG CAG GCC CAT ATG GCT AAC GAG CTG AAG CAG ATG
 A T V A Q A H M A N E L K Q M
 CAG GAC AAG TAC TCC AAA AGT GGC ATT GCT TGT TTC TTA AAA GAA
 Q D K Y S K S G I A C F L K E
 GAT GAC AGT TAT TGG GAC CCC AAT GAC GAA GAG AGT ATG AAC AGC
 D D S Y W D P N D E E S M N S
 CCC TGC TGG CAA GTC AAG TGG CAA CTC CGT CAG CTC GTT AGA AAG
 P C W Q V K W Q L R Q L V R K
 ATG ATT TTG AGA ACC TCT GAG GAA ACC ATT TCT ACA GTT CAA GAA
 M I L R T S E E T I S T V Q E
 AAG CAA CAA AAT ATT TCT CCC CTA GTG AGA GAA AGA GGT CCT CAG
 K Q Q N I S P L V R E R G P Q
 AGA GTA GCA GCT CAC ATA ACT GGG ACC AGA GGA AGA AGC AAC ACA
 R V A A H I T G T R G R S N T
 TTG TCT TCT CCA AAC TCC AAG AAT GAA AAG GCT CTG GGC CGC AAA
 L S S P N S K N E K A L G R K
 ATA AAC TCC TGG GAA TCA TCA AGG AGT GGG CAT TCA TTC CTG AGC
 I N S W E S S R S G H S F L S
 AAC TTG CAC TTG AGG AAT GGT GAA CTG GTC ATC CAT GAA AAA GGG
 N L H L R N G E L V I H E K G
 TTT TAC TAC ATC TAT TCC CAA ACA TAC TTT CGA TTT CAG GAG GAA
 F Y Y I Y S Q T Y F R F Q E E
 ATA AAA GAA AAC ACA AAG AAC GAC AAA CAA ATG GTC CAA TAT ATT
 I K E N T K N D K Q M V Q Y I
 TAC AAA TAC ACA AGT TAT CCT GAC CCT ATA TTG TTG ATG AAA AGT
 Y K Y T S Y P D P I L L M K S
 GCT AGA AAT AGT TGT TGG TCT AAA GAT GCA GAA TAT GGA CTC TAT
 A R N S C W S K D A E Y G L Y
 TCC ATC TAT CAA GGG GGA ATA TTT GAG CTT AAG GAA AAT GAC AGA
 S I Y Q G G I F E L K E N D R
 ATT TTT GTT TCT GTA ACA AAT GAG CAC TTG ATA GAC ATG GAC CAT
 I F V S V T N E H L I D M D H
 GAA GCC AGT TTT TTC GGG GCC TTT TTA GTT GGC TAA
 E A S F F G A F L V G *

FIG. 6

Expression and processing of a *trc* promoter-driven *ompA*-TNF α fusion gene product in JM109 bacteria.

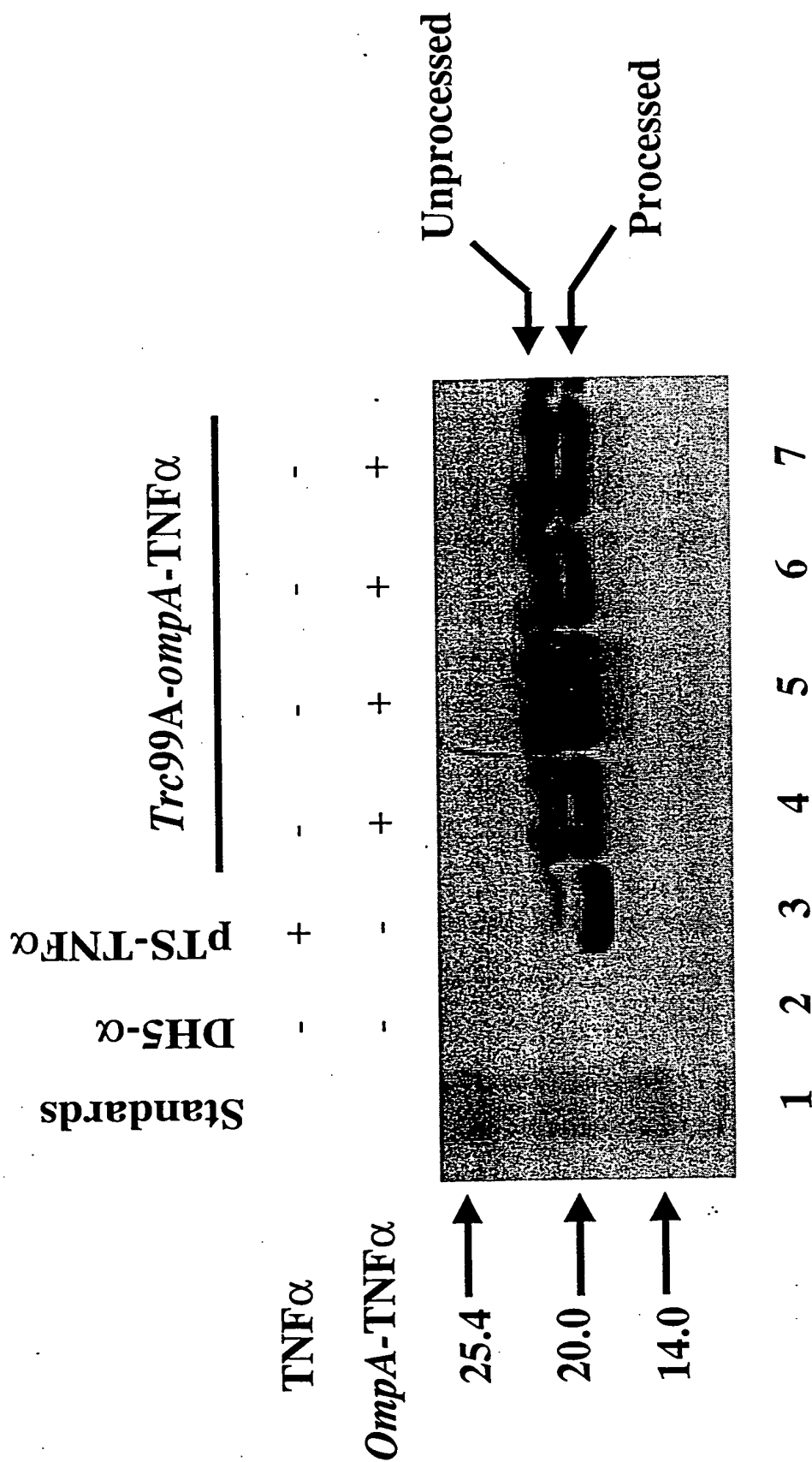


FIG. 7

ATG	AAA	AAG	ACG	GCT	CTG	GCG	CTT	CTG	CTC	TTG	CTG	TTA	GCG	CTG
M	K	K	T	A	L	A	L	L	L	L	L	L	A	L
ACT	AGT	GTA	GCG	CAG	GCC	GCT	CCT	ACT	AGC	TCG	AGC	ACT	AAG	AAA
T	S	V	A	Q	A	A	P	T	S	S	S	T	K	K
ACT	CAA	CTG	CAA	TTG	GAG	CAT	CTG	CTG	CTG	GAT	CTG	CAG	ATG	ATT
T	Q	L	Q	L	E	H	L	L	L	D	L	Q	M	I
CTG	AAT	GGC	ATC	AAT	AAC	TAC	AAG	AAC	CCT	AAG	CTG	ACT	CGC	ATG
L	N	G	I	N	N	Y	K	N	P	K	L	T	R	M
CTG	ACT	TTC	AAA	TTC	TAC	ATG	CCG	AAA	AAG	GCT	ACC	GAG	CTC	AAA
L	T	F	K	F	Y	M	P	K	K	A	T	E	L	K
CAT	CTC	CAG	TGC	CTG	GAA	GAG	GAA	CTG	AAG	CCG	CTG	GAG	GAA	GTA
H	L	Q	C	L	E	E	E	L	K	P	L	E	E	V
CTT	AAC	CTG	GCA	CAG	TCT	AAG	AAC	TTC	CAC	CTG	CGT	CCG	CGT	GAC
L	N	L	A	Q	S	K	N	F	H	L	R	P	R	D
CTG	ATC	TCC	AAC	ATC	AAT	GTA	ATC	GTT	CTT	GAG	CTG	AAG	GGA	TCC
L	I	S	N	I	N	V	I	V	L	E	L	K	G	S
GAA	ACC	ACC	TTC	ATG	TGC	GAA	TAC	GCT	GAC	GAA	ACC	GCC	ACC	ATT
E	T	T	F	M	C	E	Y	A	D	E	T	A	T	I
GTG	GAG	TTC	CTG	AAC	CGT	TGG	ATC	ACC	TTT	GCC	CAA	TCG	ATC	ATT
V	E	F	L	N	R	W	I	T	F	A	Q	S	I	I
AGC	ACG	TTA	ACT	TAA										
S	T	L	T	*										

FIG. 8

Periplasmic localization and processing of *ompA*-IL2 fusion proteins.

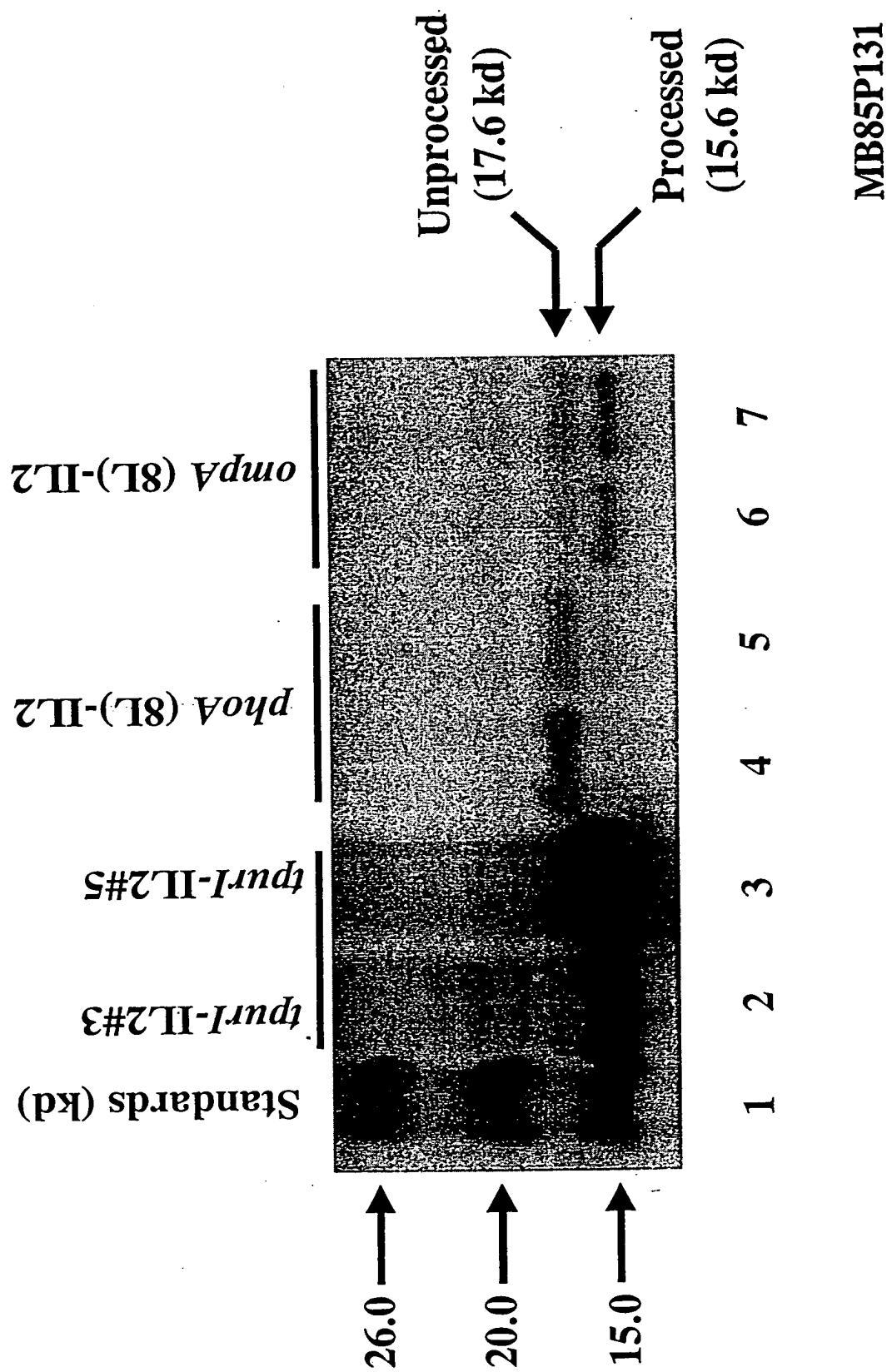


FIG. 9

ATG	AAA	CAG	TCG	ACT	CTG	GCG	CTT	CTG	CTC	TTG	CTG	TTA	GCG	CTG
M	K	Q	S	T	L	A	L	L	L	L	L	L	A	L
ACT	AGT	GTG	GCC	AAA	GCG	GCT	CCT	ACT	AGC	TCG	AGC	ACT	AAG	AAA
T	S	V	A	K	A	A	P	T	S	S	S	T	K	K
ACT	CAA	CTG	CAA	TTG	GAG	CAT	CTG	CTG	CTG	GAT	CTG	CAG	ATG	ATT
T	Q	L	Q	L	E	H	L	L	L	D	L	Q	M	I
CTG	AAT	GGC	ATC	AAT	AAC	TAC	AAG	AAC	CCT	AAG	CTG	ACT	CGC	ATG
L	N	G	I	N	N	Y	K	N	P	K	L	T	R	M
CTG	ACT	TTC	AAA	TTC	TAC	ATG	CCG	AAA	AAG	GCT	ACC	GAG	CTC	AAA
L	T	F	K	F	Y	M	P	K	K	A	T	E	L	K
CAT	CTC	CAG	TGC	CTG	GAA	GAG	GAA	CTG	AAG	CCG	CTG	GAG	GAA	GTA
H	L	Q	C	L	E	E	E	L	K	P	L	E	E	V
CTT	AAC	CTG	GCA	CAG	TCT	AAG	AAC	TTC	CAC	CTG	CGT	CCG	CGT	GAC
L	N	L	A	Q	S	K	N	F	H	L	R	P	R	D
CTG	ATC	TCC	AAC	ATC	AAT	GTA	ATC	GTT	CTT	GAG	CTG	AAG	GGA	TCC
L	I	S	N	I	N	V	I	V	L	E	L	K	G	S
GAA	ACC	ACC	TTC	ATG	TGC	GAA	TAC	GCT	GAC	GAA	ACC	GCC	ACC	ATT
E	T	T	F	M	C	E	Y	A	D	E	T	A	T	I
GTG	GAG	TTC	CTG	AAC	CGT	TGG	ATC	ACC	TTT	GCC	CAA	TCG	ATC	ATT
V	E	F	L	N	R	W	I	T	F	A	Q	S	I	I
AGC	ACG	TTA	ACT	TAA										
S	T	L	T	*										

FIG. 10

Antitumor efficacy of pTS-BrpTNF α Clone 2 in a staged
Colon 38 tumor model.

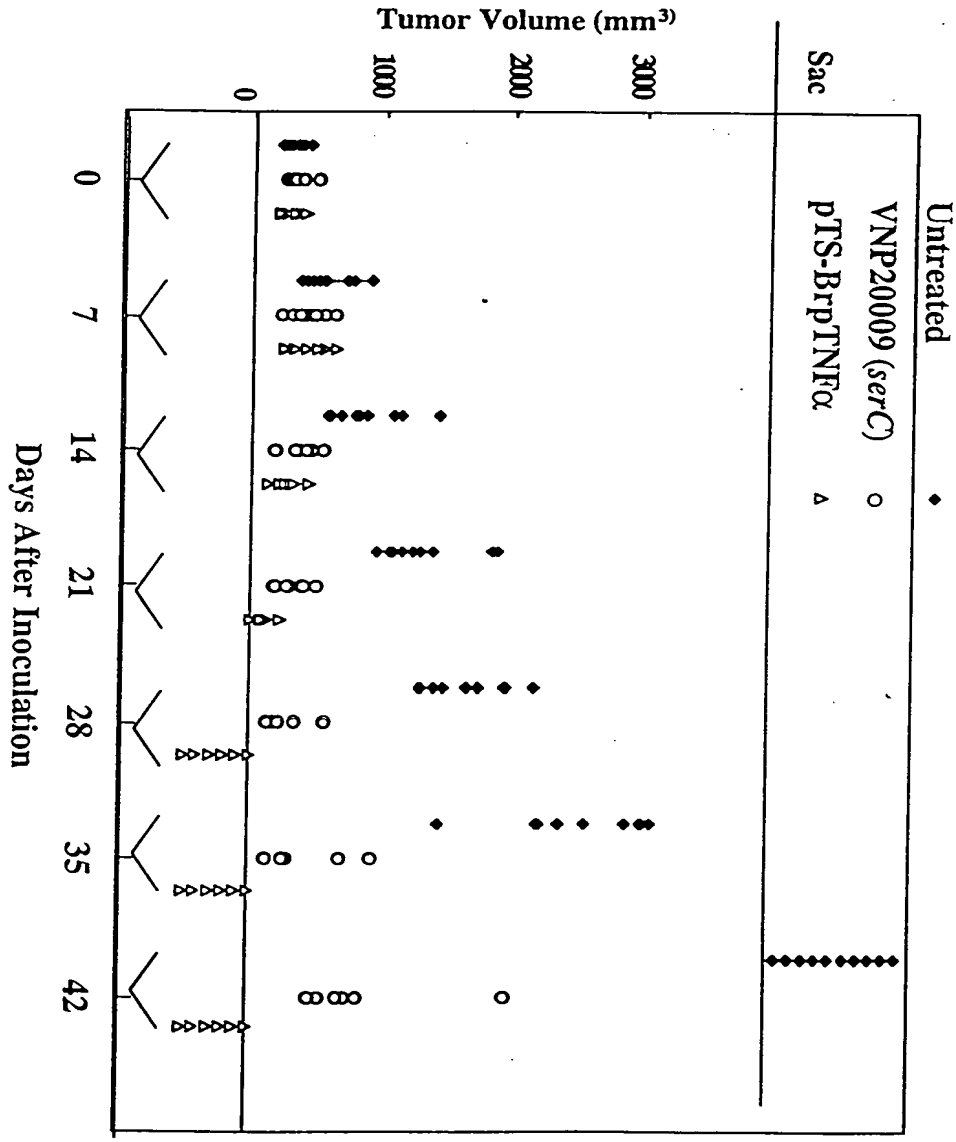


FIG. 11

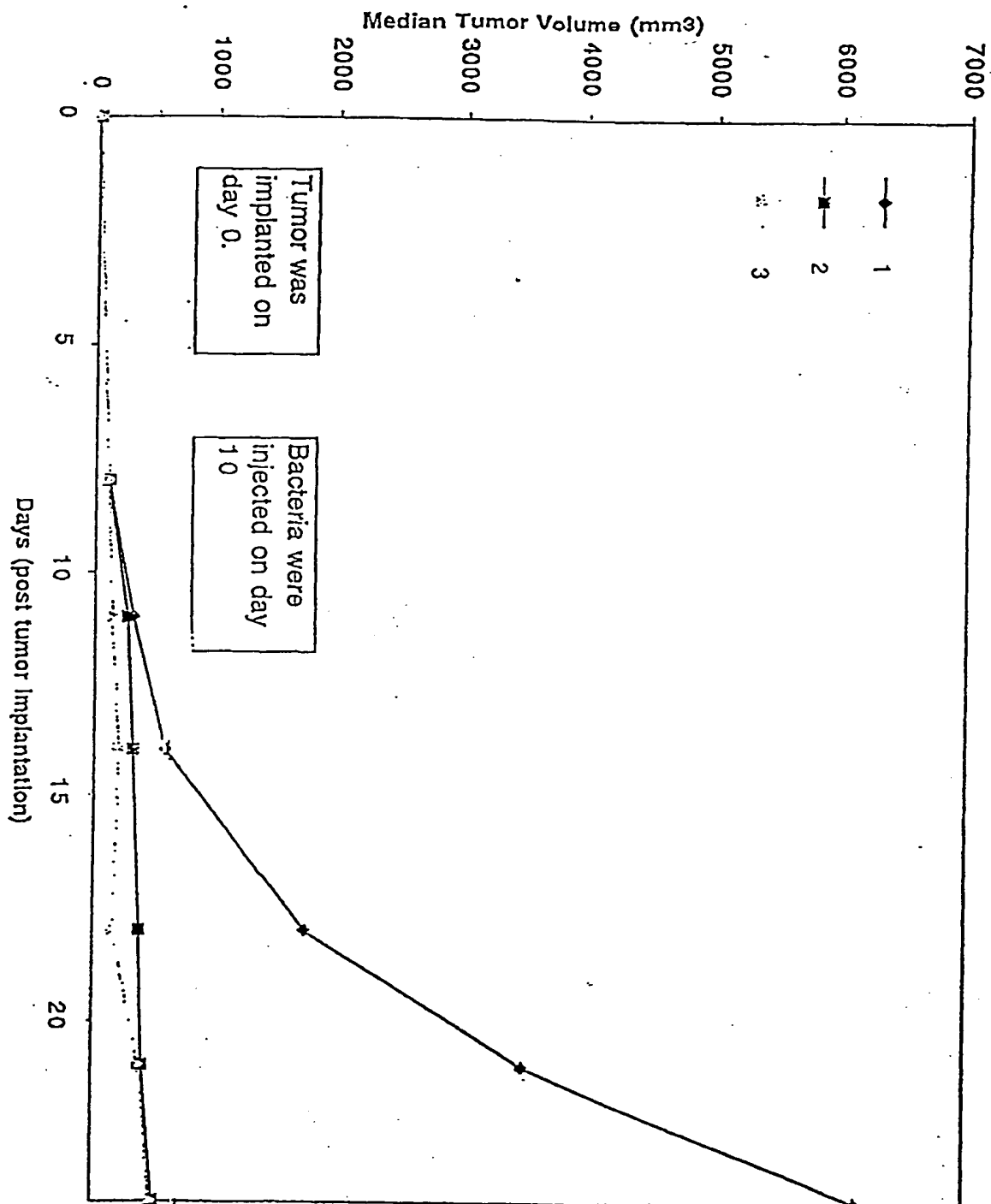


FIG. 12

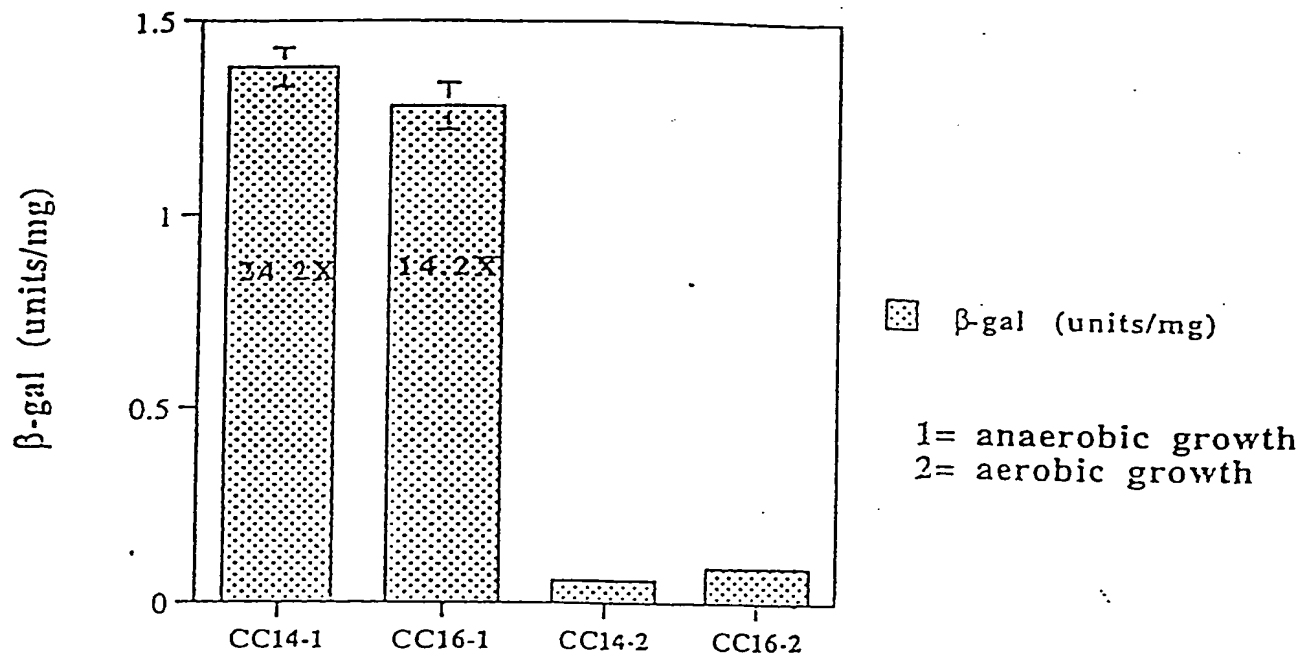
β -gal activity in strains carrying pepT/bgal

FIG. 13A

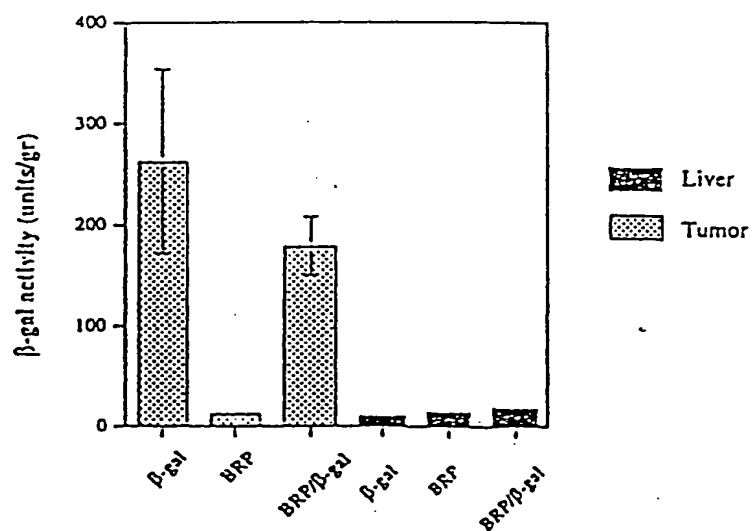
 β -gal activity *in vivo*, pepT β -gal \pm BRP

FIG. 13B

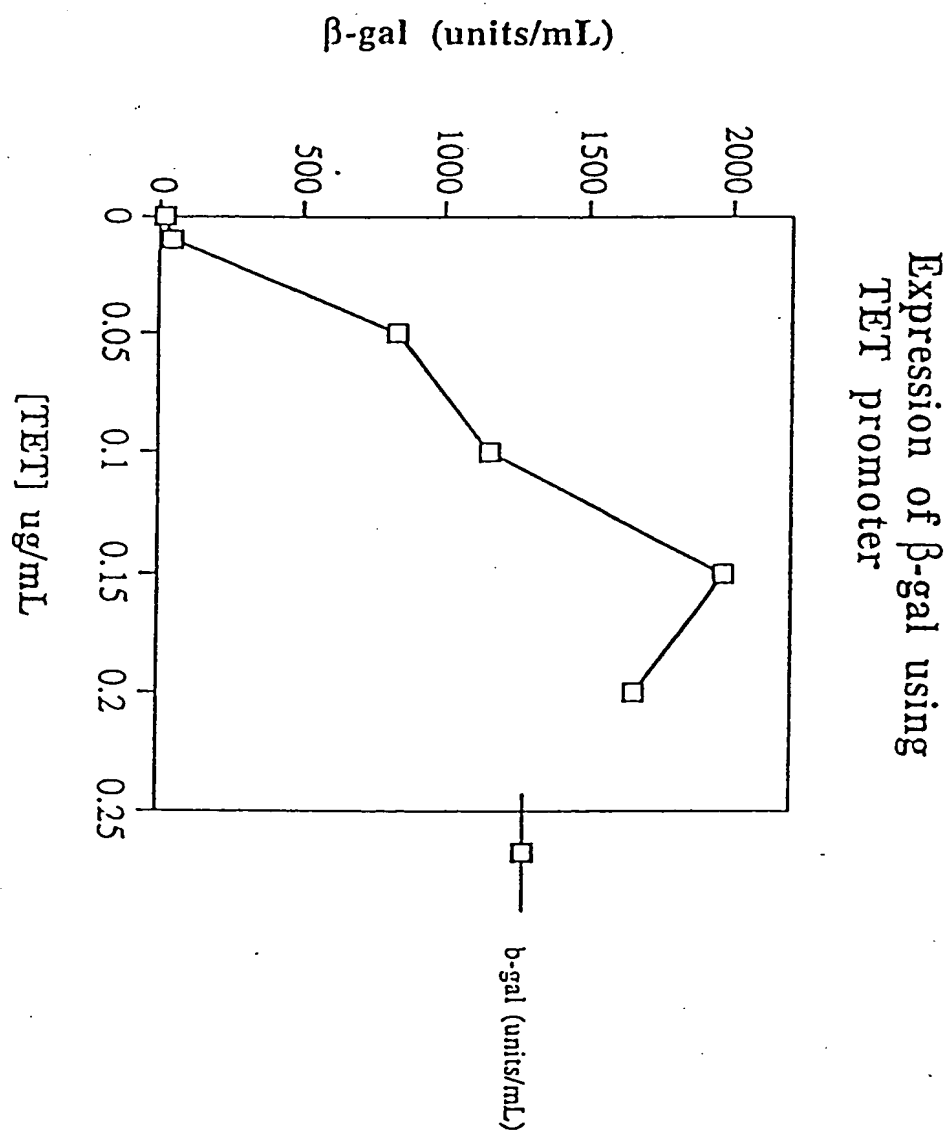
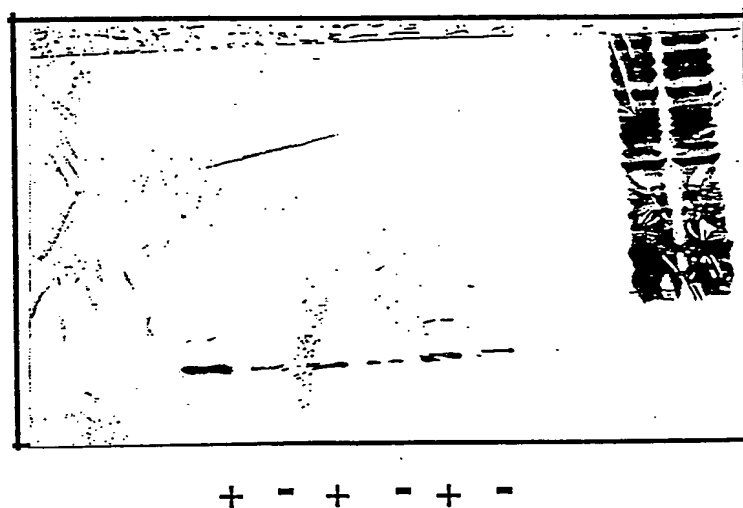


FIG. 14

A.

~25 kD →
HexaHIS-endostatin



B.

~25 kD →
HexaHIS-endostatin

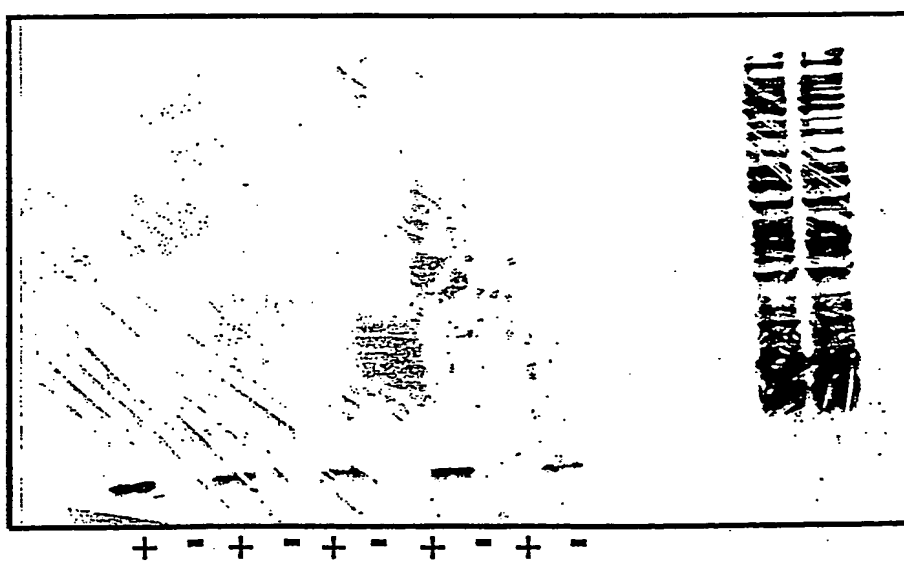


FIG. 15

~25kD
HexaHIS-endostatin

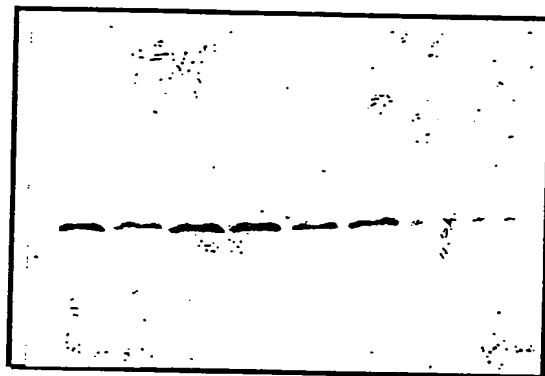


FIG. 16

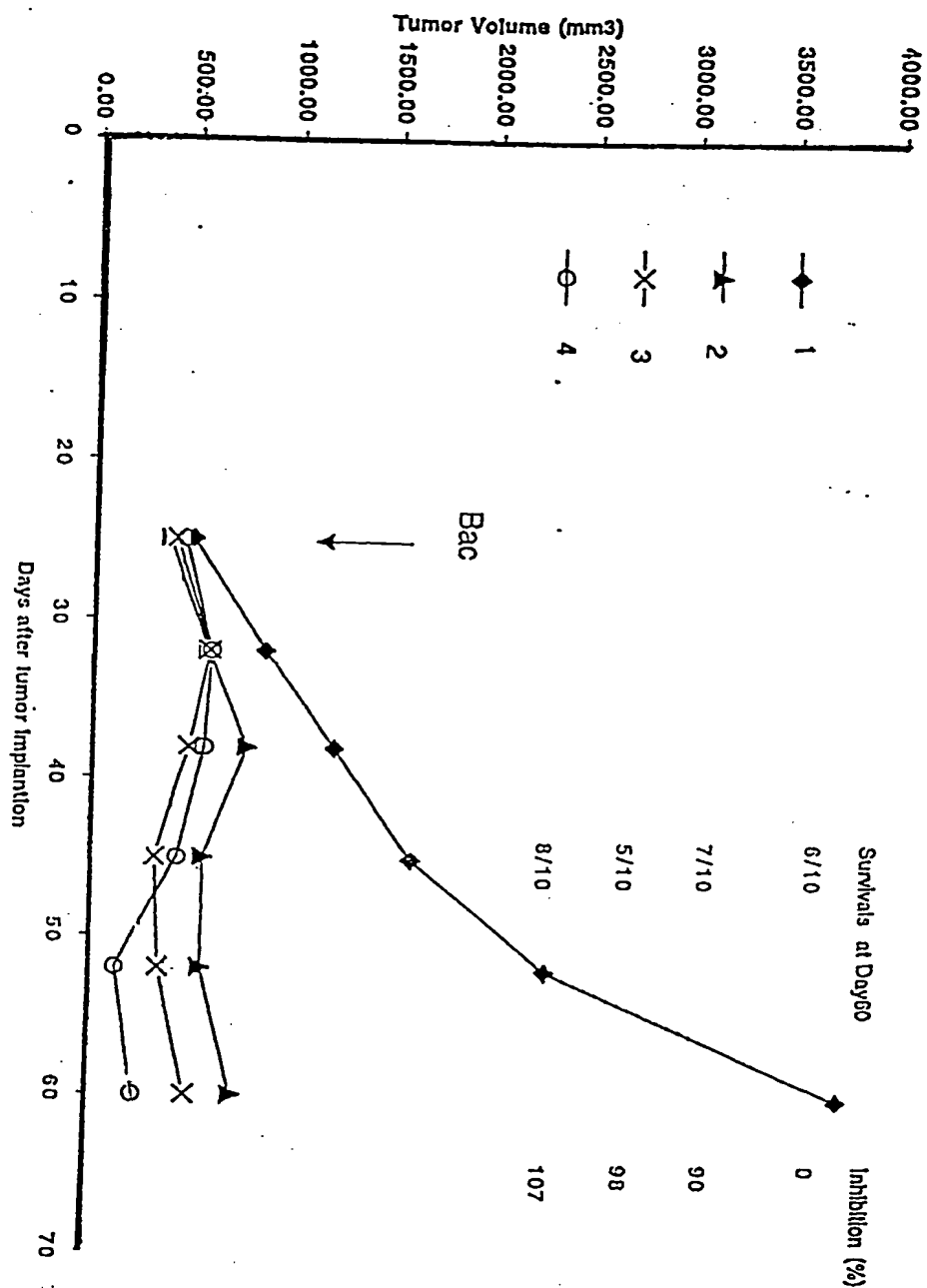


FIG. 17

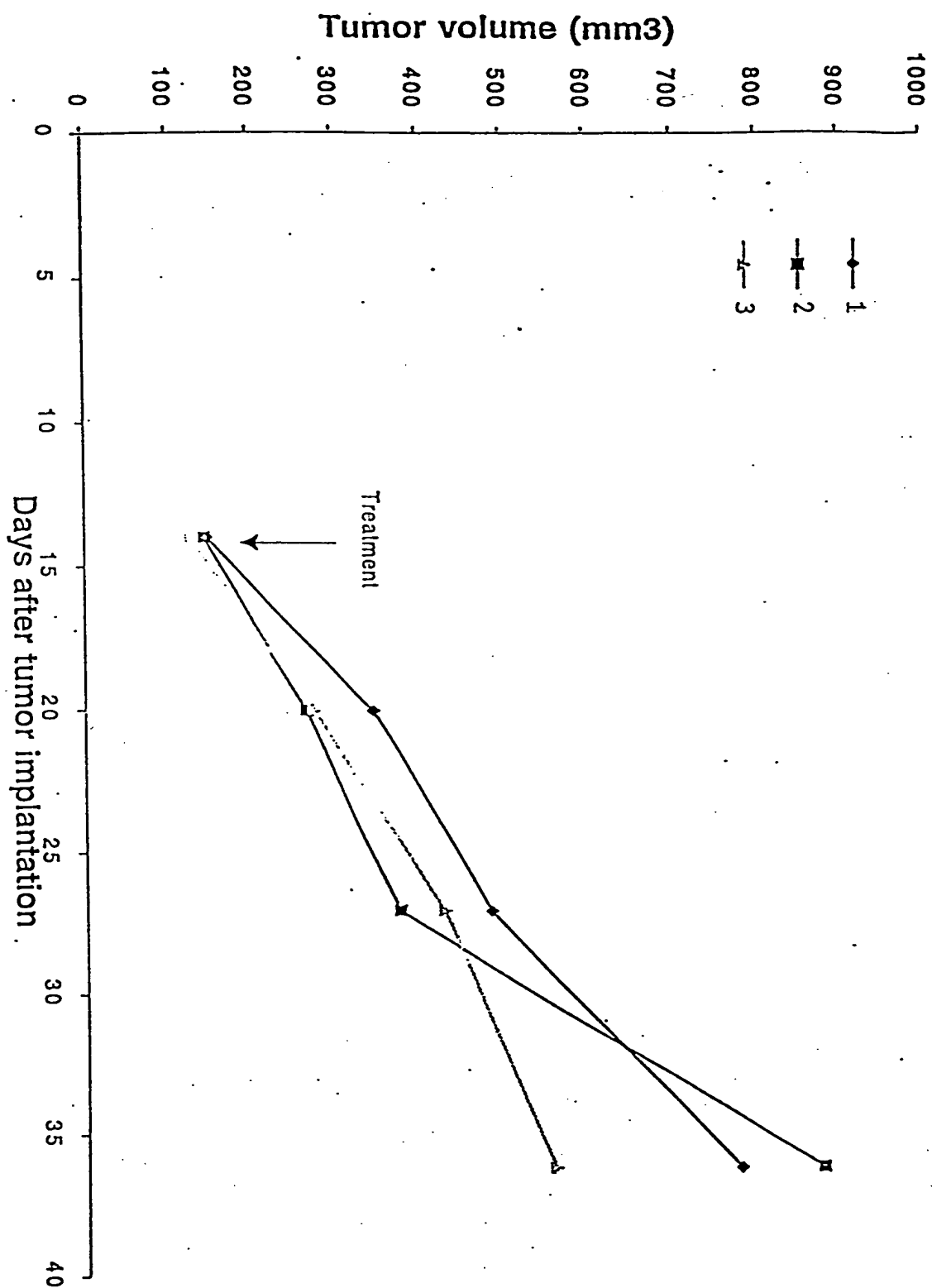
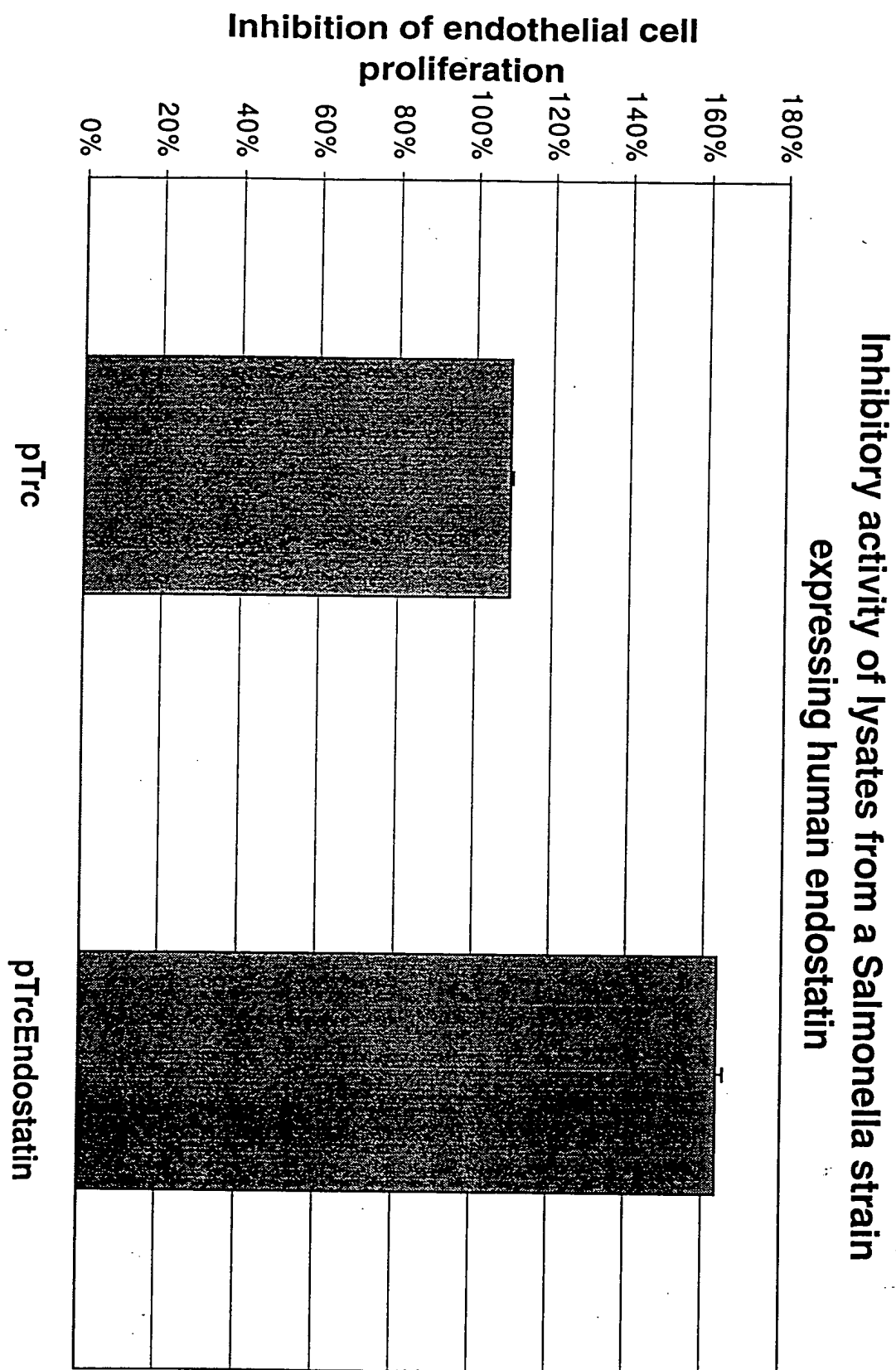
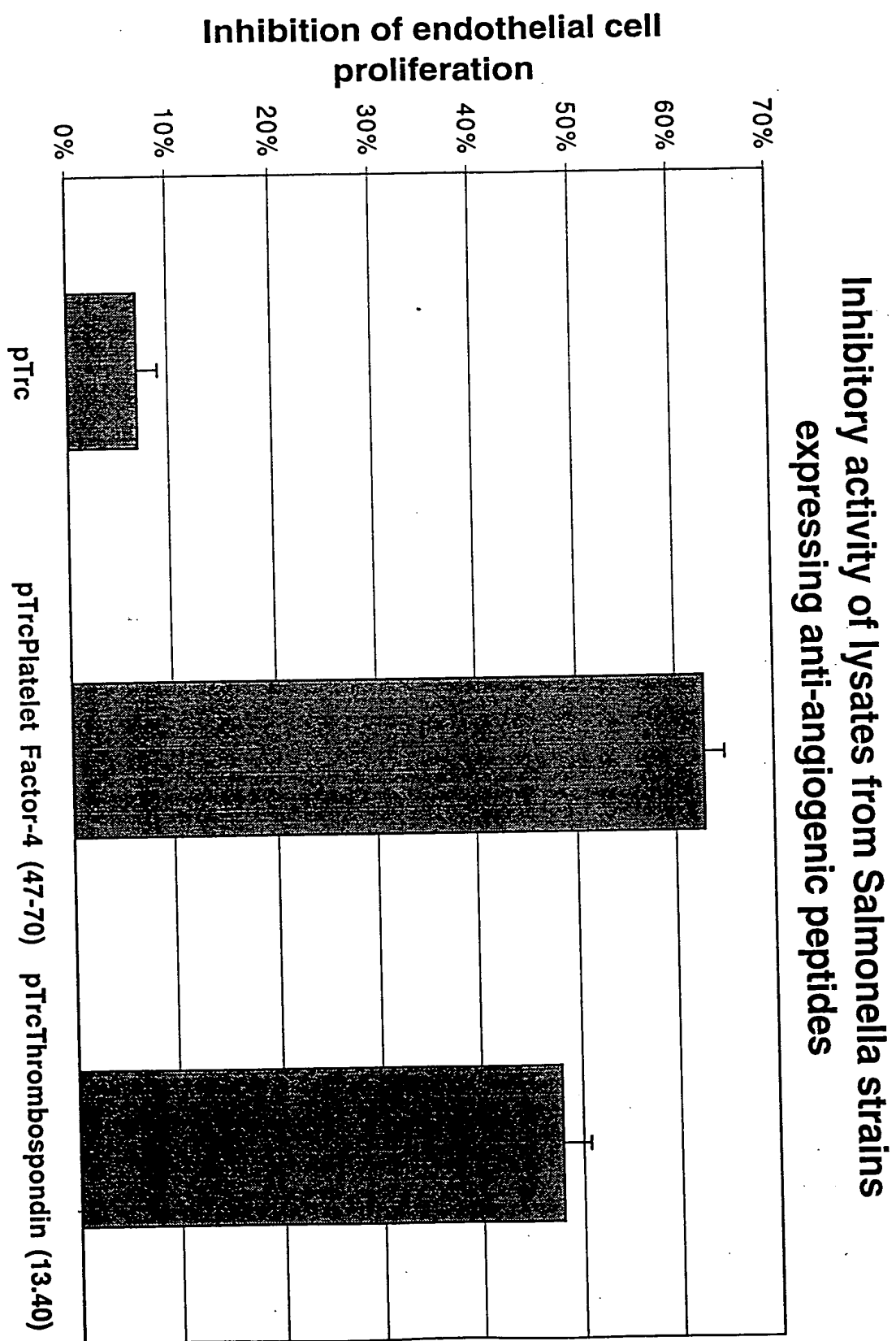


FIG. 18

**FIG. 19**

**FIG. 20**

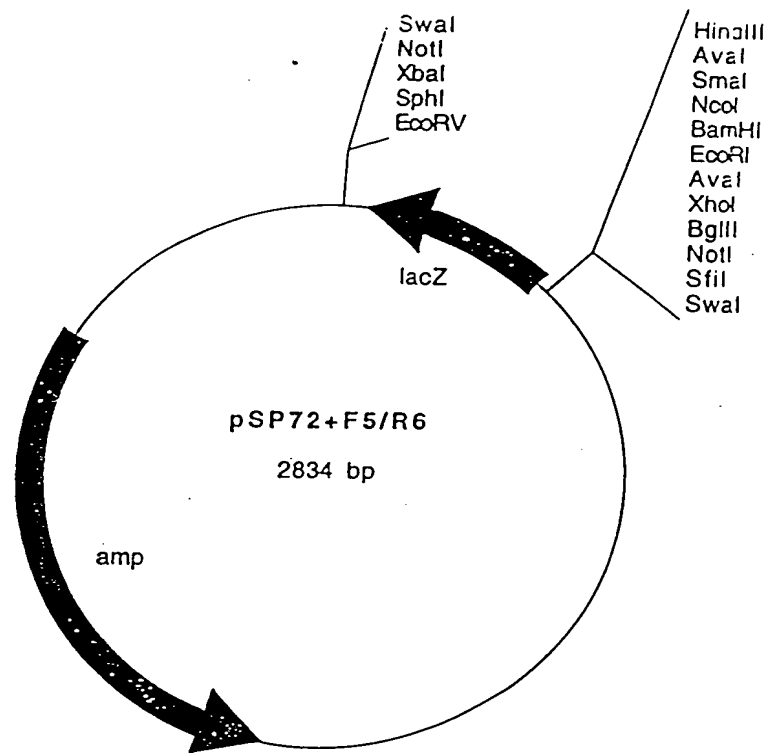


FIG. 21

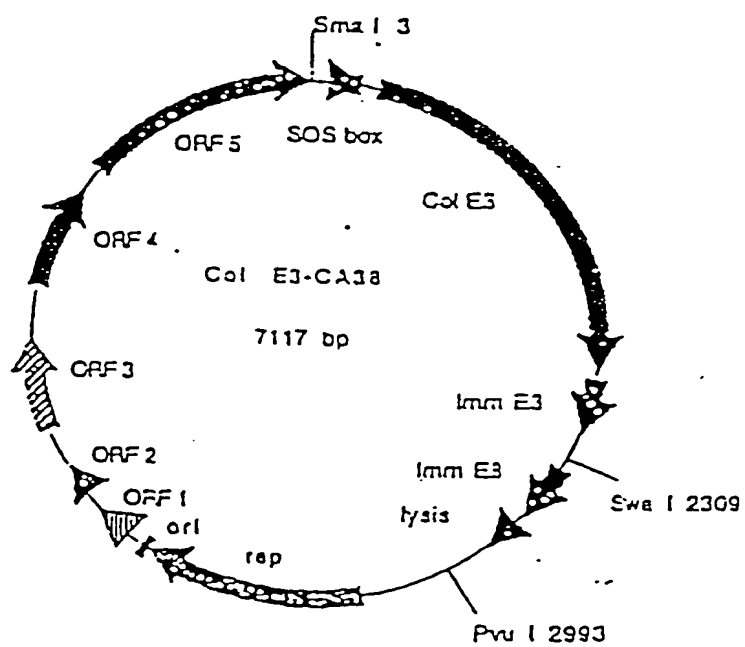
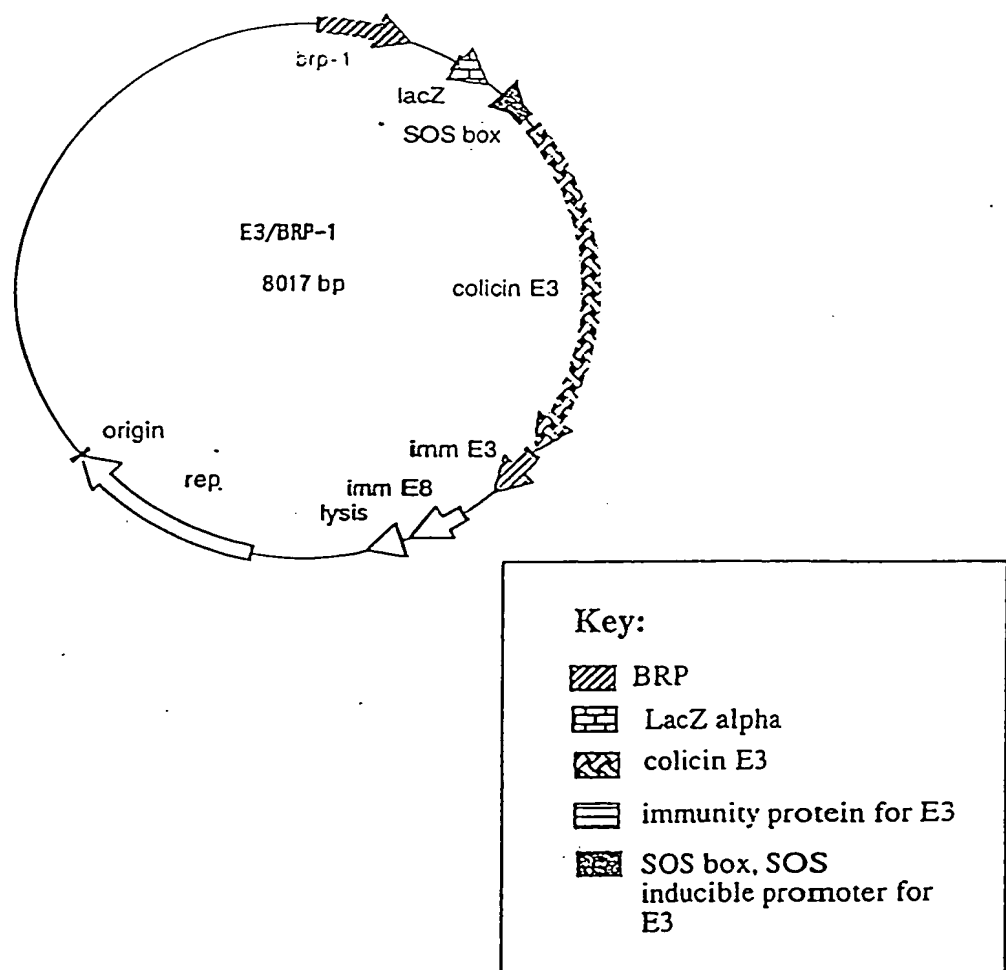
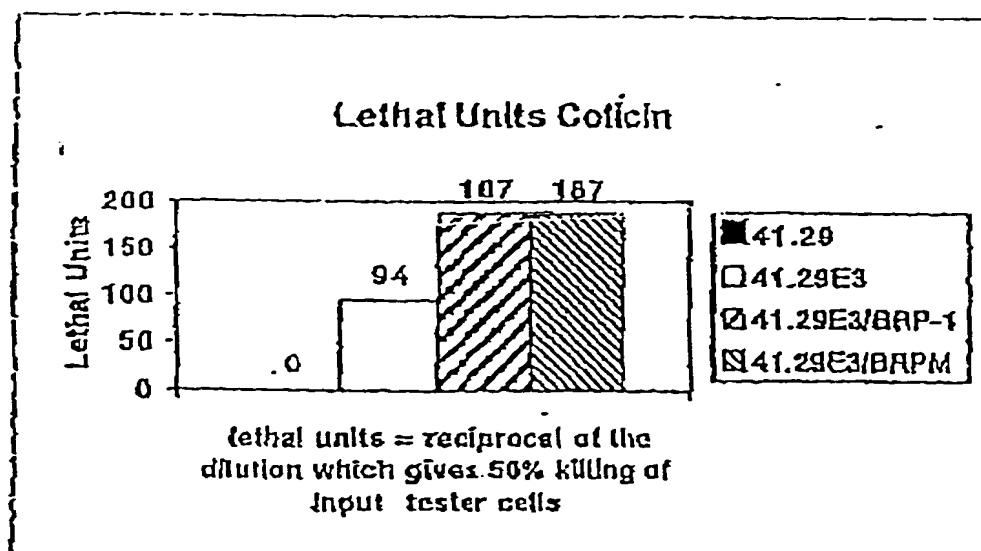


FIG. 22

**FIG. 23**

**FIG. 24**

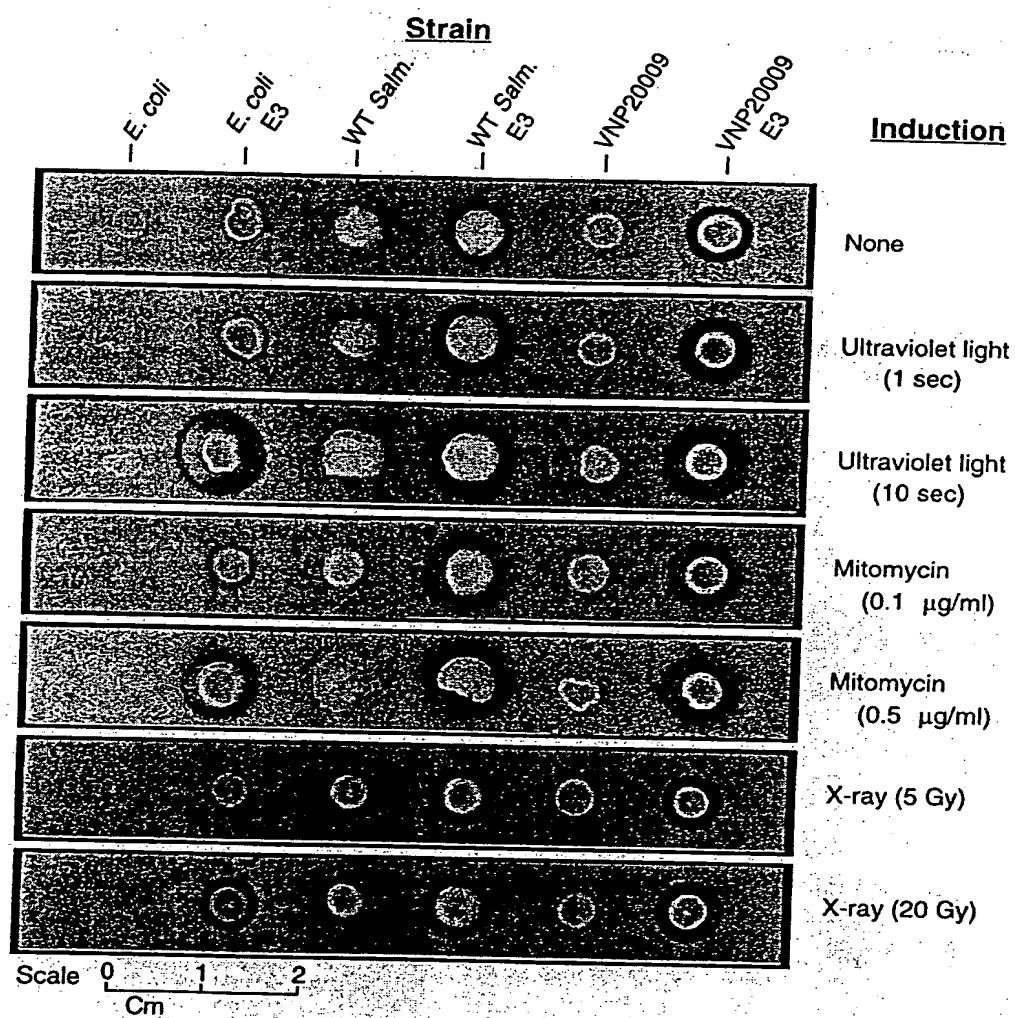


FIG. 25

Efficacy of 41.2.9/ColE3 on C38 Murine Colon Carcinoma

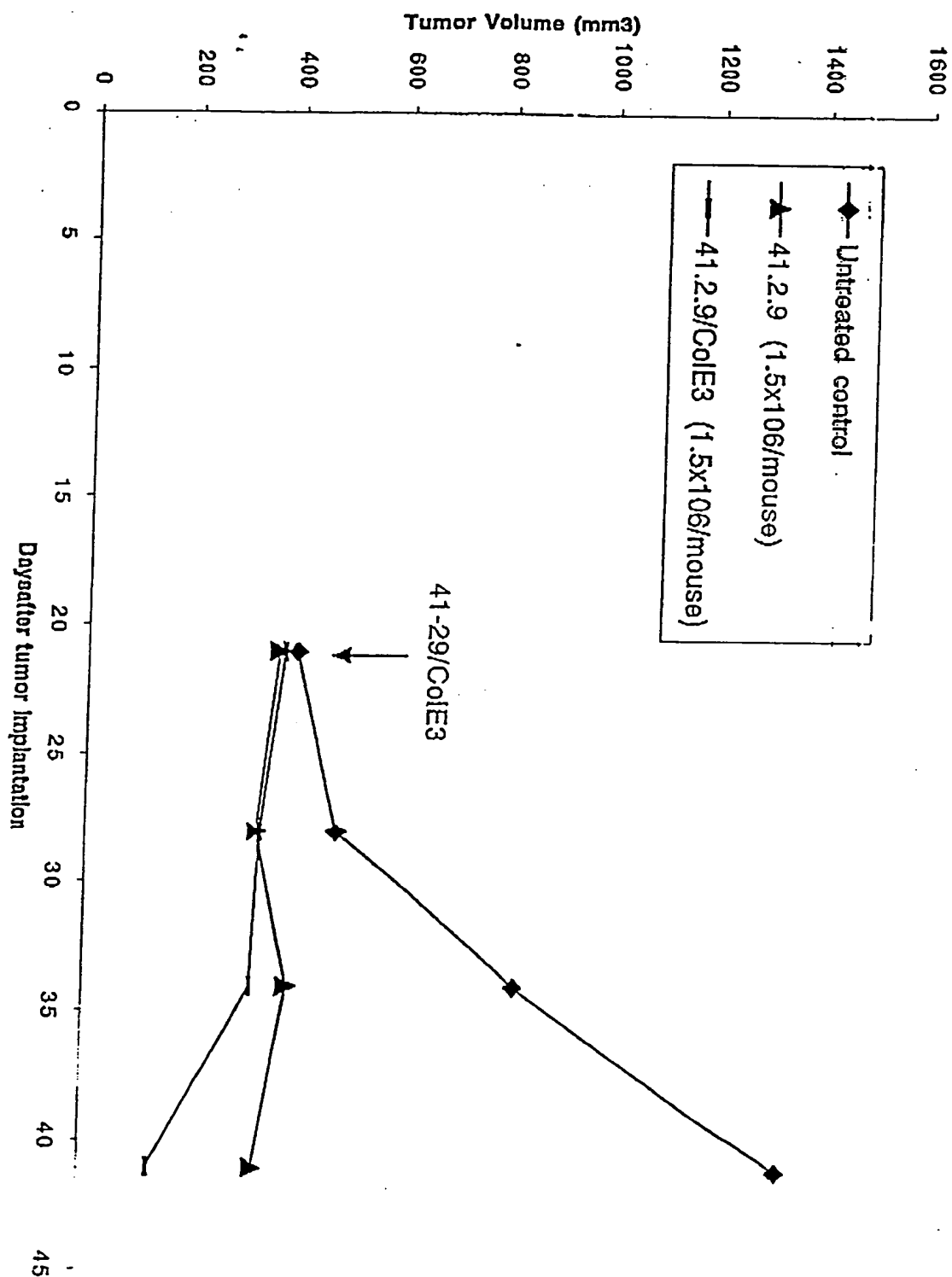


FIG. 26

Anti-tumor Activity of 41.2.9 /Col/E3 on DLD1 Human Colon Carcinoma in
Nu/Nu Mice

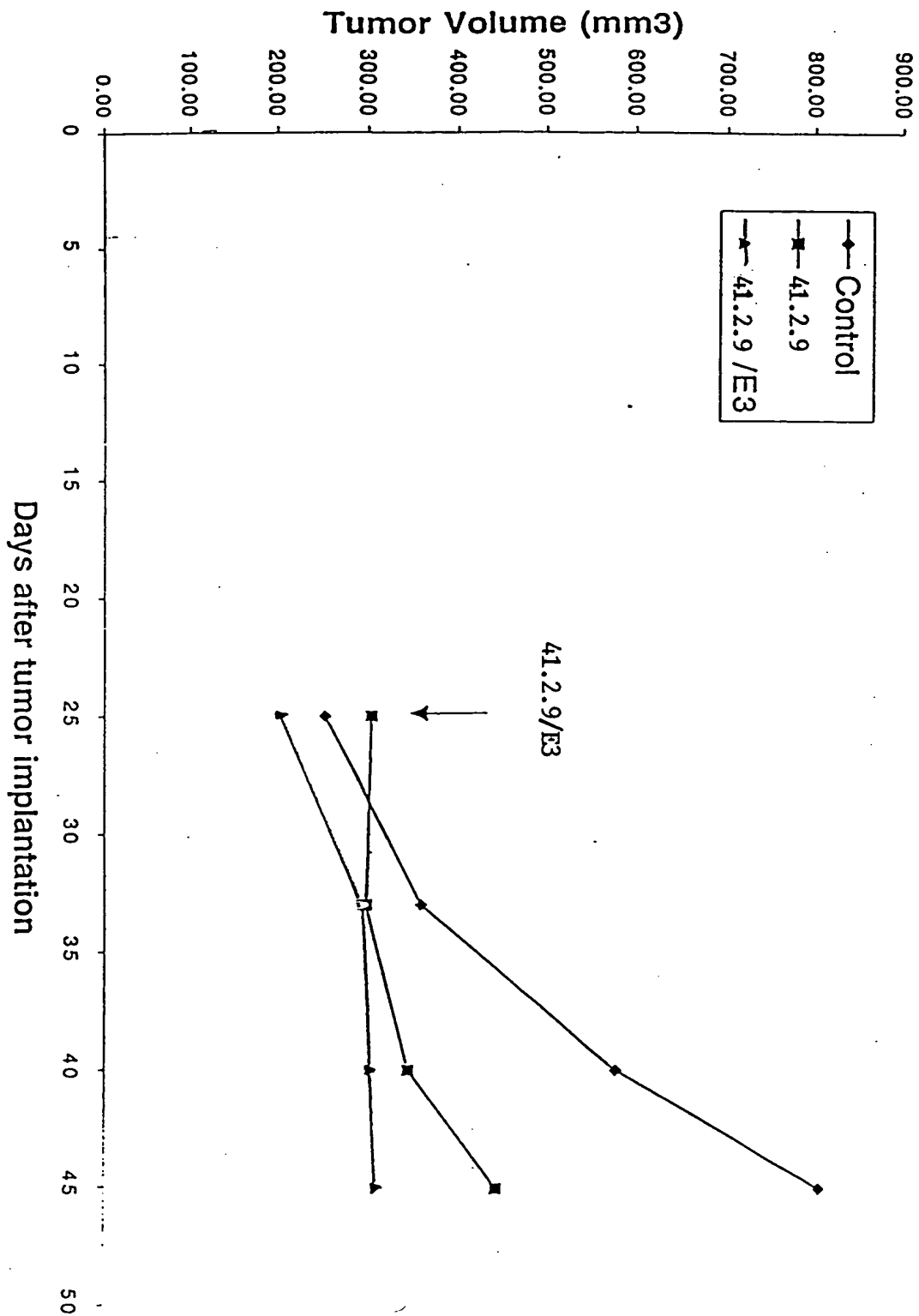


FIG. 27

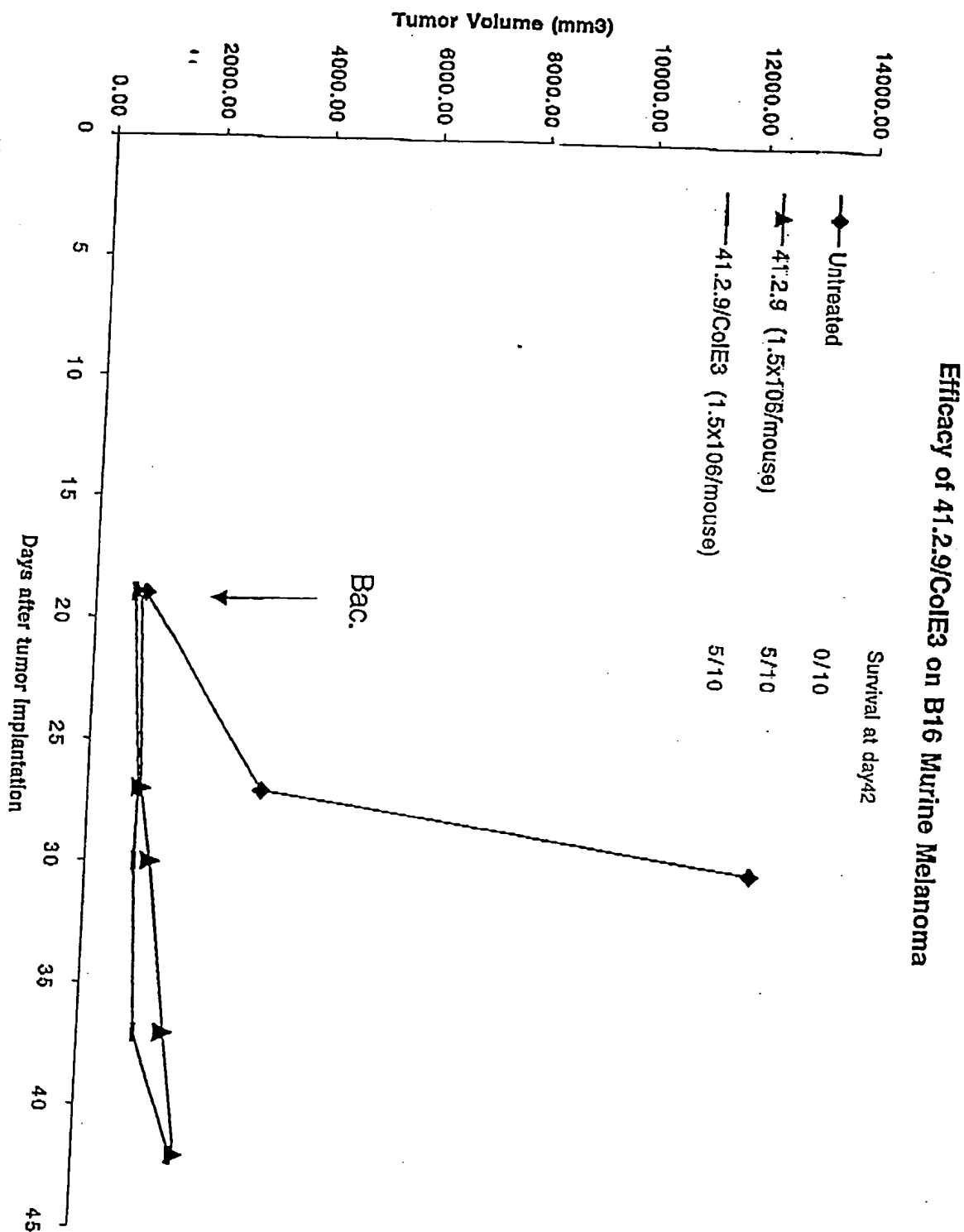
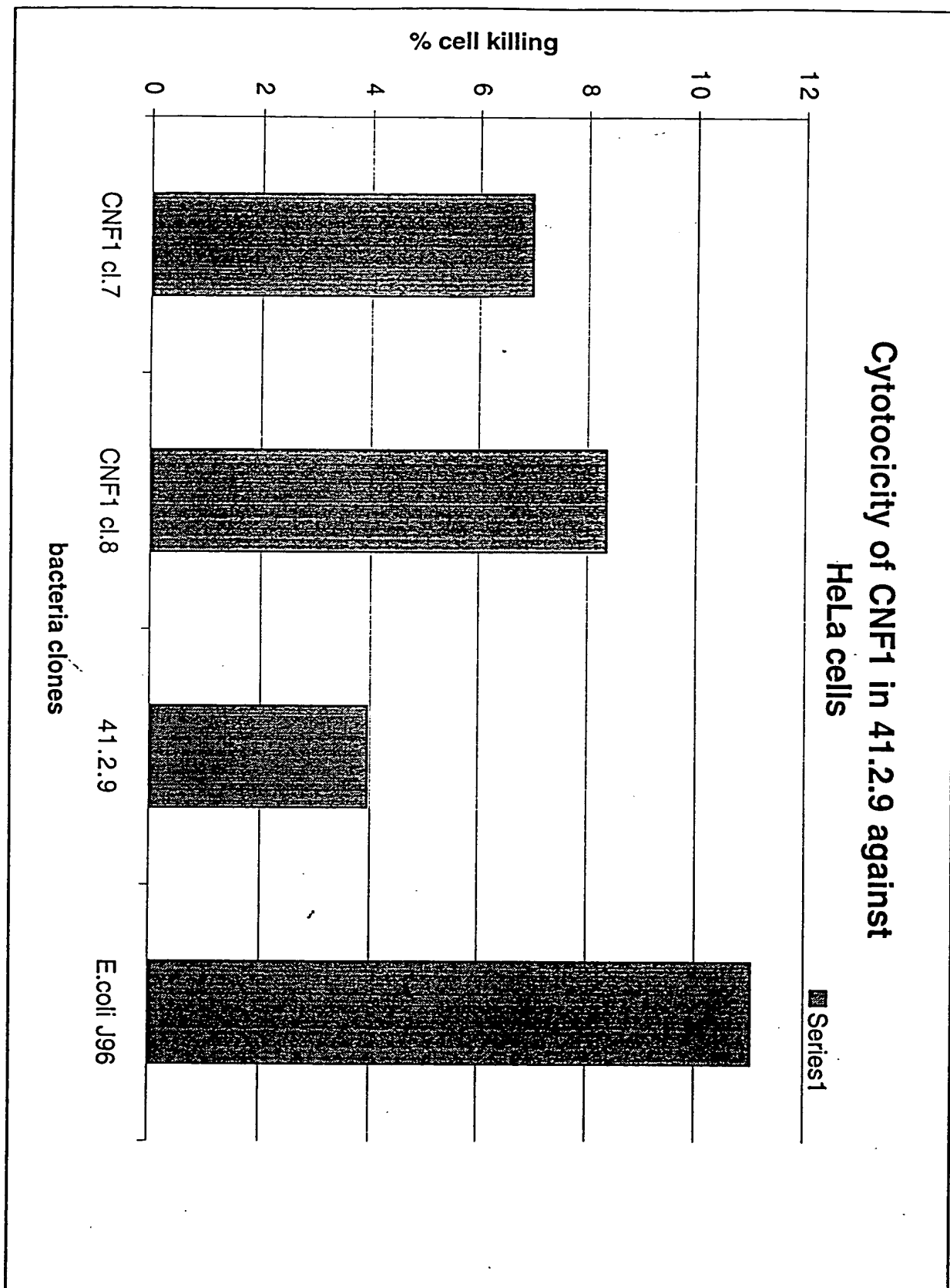
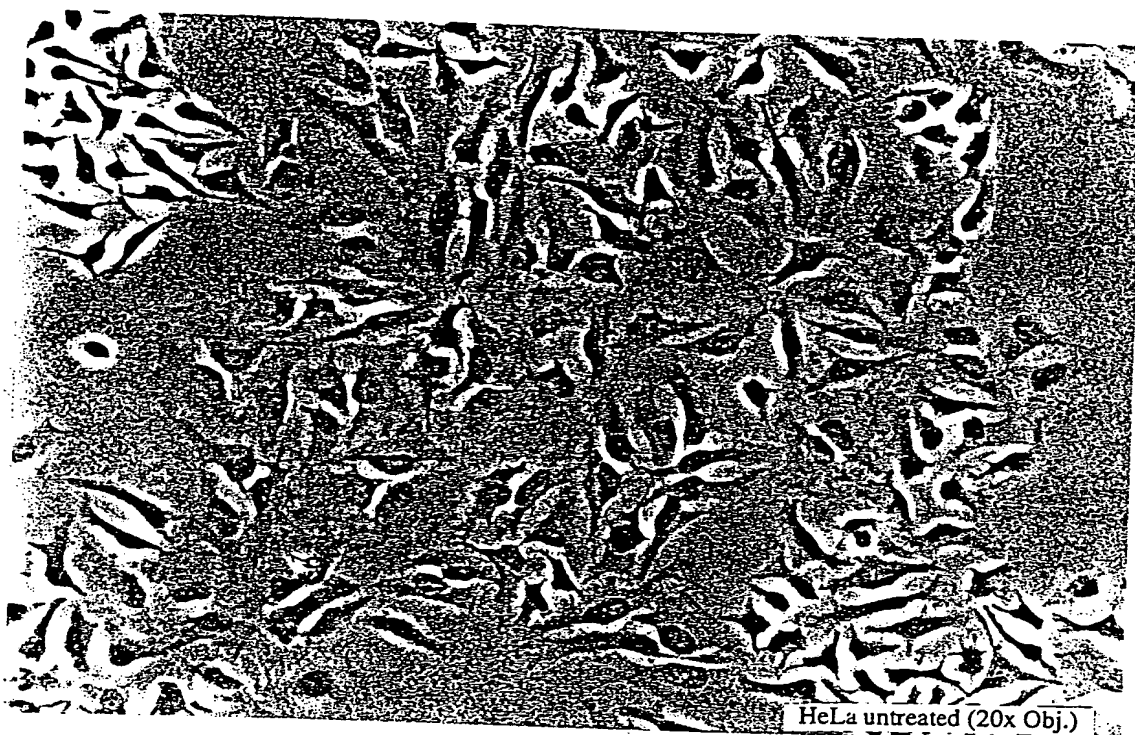
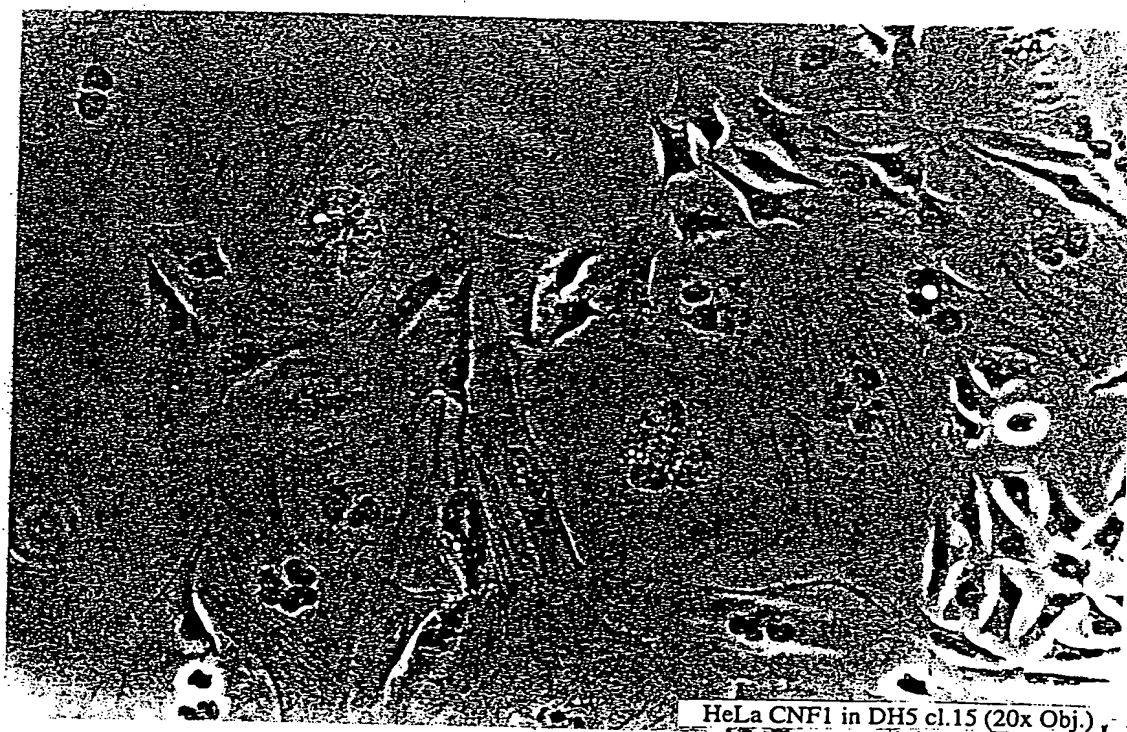


FIG. 28

**FIG. 29**

A**B****FIG. 30**

GATATCATTG	TGGCCTCTGA	CGTTGTGATG	GTCGCACGTS	GCGATCTGGG	CGTTGAAATC	GCGGATCCGG	70
AGCTGGTTGG	TATCCAGAAA	GCGCTGATTG	GCCGTGCGCG	TCAGCTAAAC	CGCGCAGTCA	TCACCGCAAC	140
GCAAATGATG	GAGTCGATGA	TCACCAACCC	GATGCCGACC	CGTGCGGAAG	TGATGGACGT	GCGGAACGCC	210
GTCTTGATG	GCACGGATGC	GGTTATGCTG	TCTGCCGAAA	CCGCAGCCGG	TCAGTATCCT	TCTGAAACCG	280
TTGCCGCAAT	GCGCGCGGTC	TGCCTGGGCG	CAGAAAAAAT	CCCCAGCATC	AATGTGTCTA	AACACCGTCT	350
CGACGTGCAG	TTGACAACG	TTGAAGAAGC	CATTGCCATG	TCTGCGATGT	ATGCGGCAAA	CCATCTGAAA	420
GCGGTTACCG	CGATCATCAC	CATGACGGAA	TCCGGTCGTA	CCGCGCTAAT	GACTTCCCGT	ATCAGCTCCG	490
GCCTGCCGAT	TTTGCCCATG	TCGCGCCATG	AACGCACGCT	GAACCTGACC	GCGCTCTATC	GCGGAGTAAC	560
GCCGTTGCAT	TTTGATAGCG	CGGCTGATGG	CGTTGTGCGG	GCACATGAAG	CTGTTAATCT	GCTGCGCGAT	630
AAAGGGTATC	TGGTTTCCGG	CGACCTGGTT	ATCGTGACCC	AGGGCGATGT	CATGAGCACC	GTCGGTTCAA	700
CCAATACCAC	GCGGCCGCCC	CCTTAATTAA	CCCCGCATGC	GGGGGGCCAT	ATAGGCCGGG	GATTTAAATG	770
CAAACGTCCG	CCGAAACGCC	GACGCACTGT	GTTCCAGATA	TAGTCAAAAA	CCGGATTACC	CTGATTATGA	840
AACATCGCCG	CCATTTTGTG	CCCCTGAGAG	GCCATCAGCA	TGGCTGGAAT	GTCGACGCCC	CAGCCATGCG	910
GTACGAGAAA	AATGACTTTT	TCGTGCTTAC	GACGCATCTC	CTCGATAATC	TCCAGACCTT	CCCAGTCAAC	980
ACGCTGTTGA	ATTTTMTTCG	GACCGCGCAT	CGCCAACTCA	GCCATCATCG	CCATTGCCTG	TGGCGCGGTG	1050
GCGAACATCT	CATCGACAAT	CGCTTCGCGC	TCAGCTTCGC	TACGCTGCGG	AAAGCACAAAC	GACAGATTAA	1120
TTAGCGCCCG	GCGACGAGAA	CTCTTCCCCA	GCCGTCCGGC	AAAACGCCCC	AGCGTCGCCA	GCAAAGGGTC	1190
GCGGAATGAT	GCCGGTGTGA	ATGCGATCCC	CGCCATGCGC	GCCGCGCCCA	ACCAGGCGCC	CCAATACTGT	1260
GGATAGCGAA	AGGATTTTTC	GAATTCAGGG	ATATACTCAC	TATTATTTTT	TTTGGTTTCC	ATGCTTTTCC	1330
AGGGTCTGCT	GACGCGAAAA	GGAATGTGA	ATAGTGTAGC	GACGCTGCGC	TCTCACACAA	AACAAAAAAG	1400
CCGGCACACA	TCGCGTACCG	GCTCTGTCAG	CGCATTTGTT	AATCGAAGCG	CAGTTGCGGC	AGAACCTCTT	1470
TCACCTGTGC	CAGGTATTCA	CGACGATCTG	ACCCCGTCAG	ACCTTCGGTG	CGCGGCAATT	TTGCTGTCAG	1530
AGGGTTAACG	GCTTGCTGGT	TGATC					1555

FIG. 31

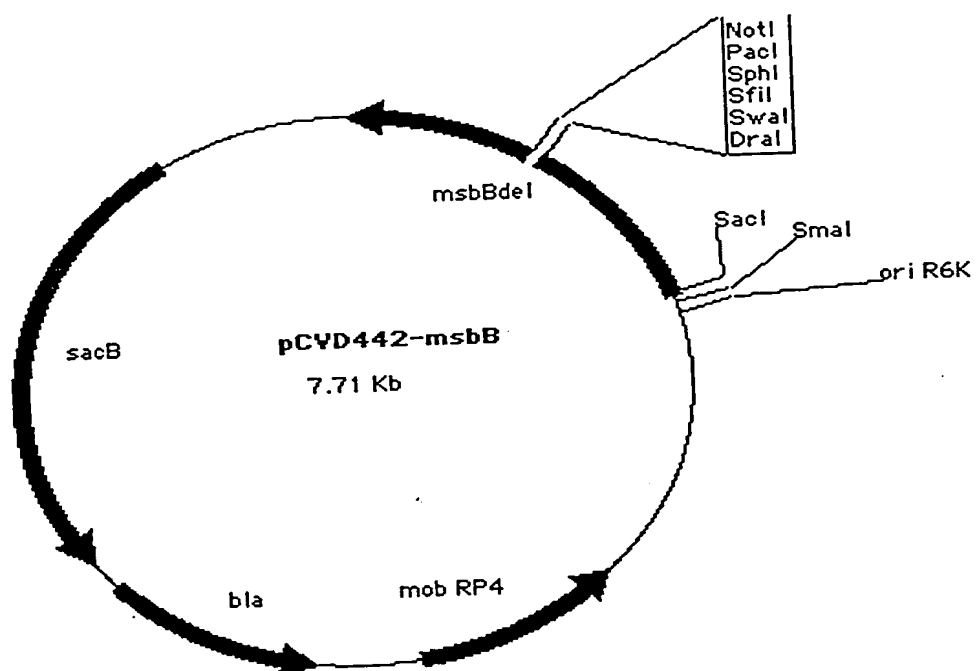


FIG. 32

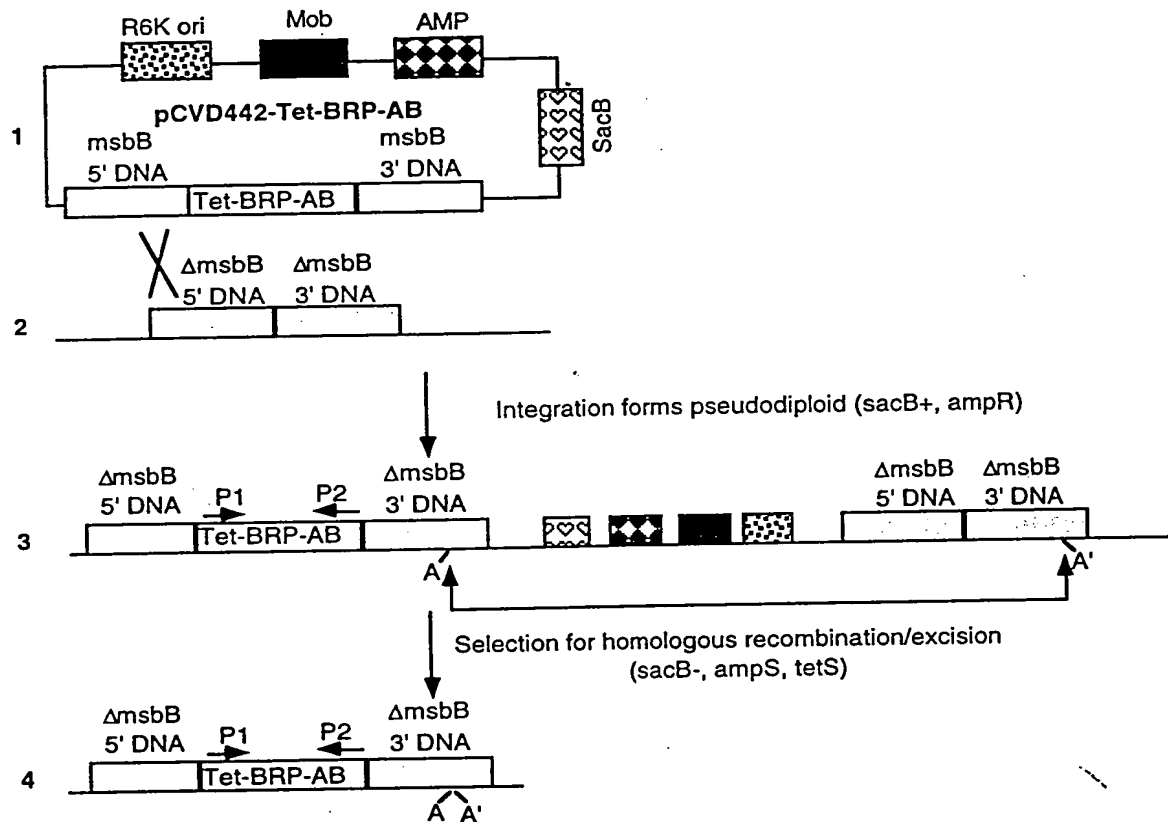


FIG.33

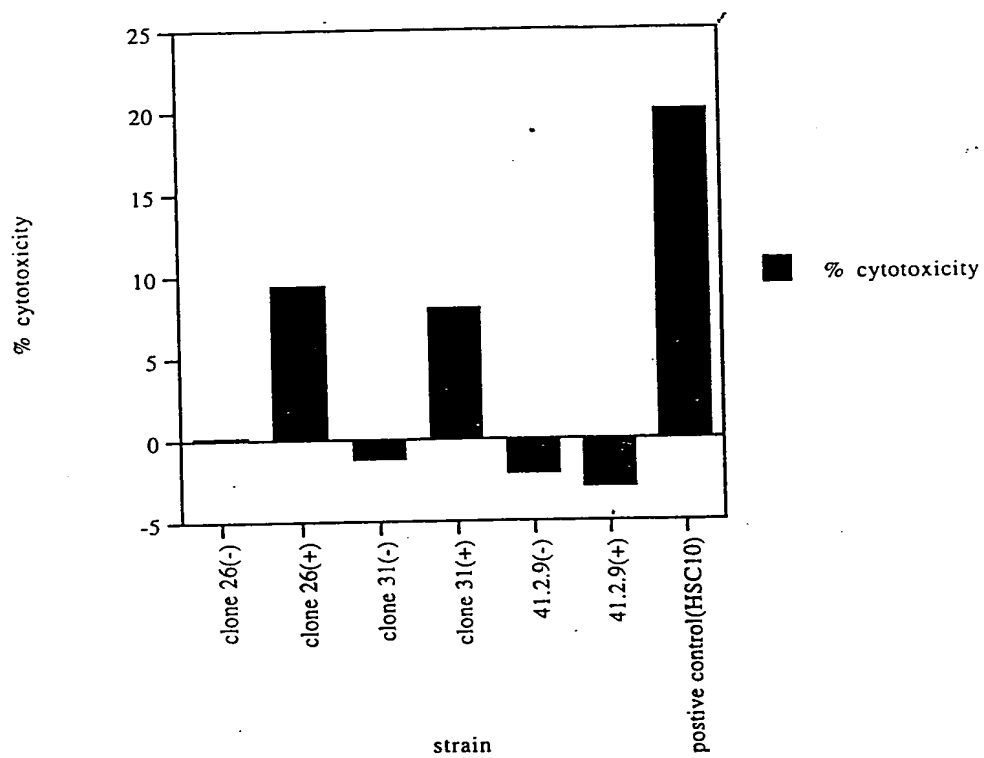


FIG. 34

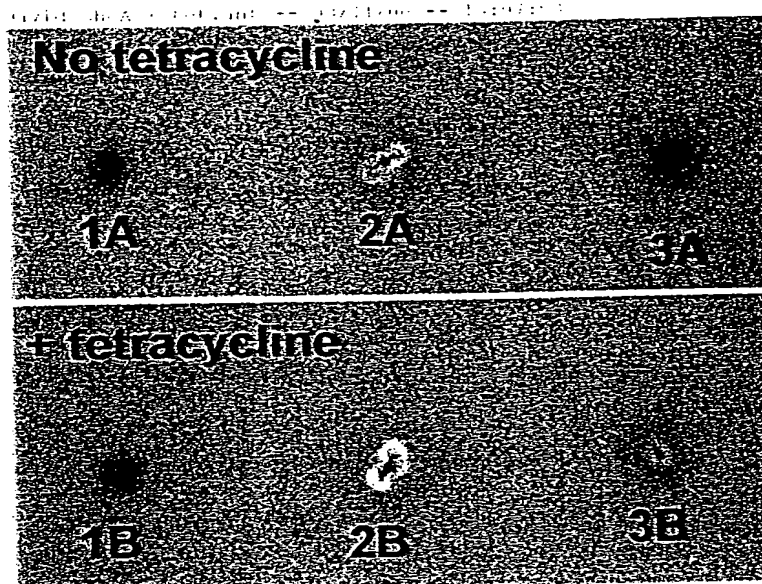
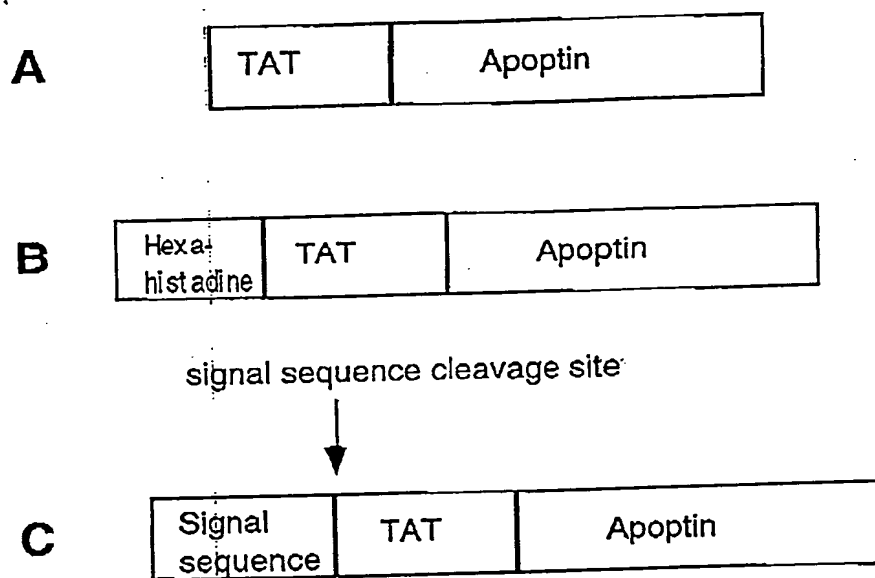


FIG. 35

**FIG. 36**

Protein Sequence of 616-4 F

page 1

Length of 616-4 F: 551 bp; Listed from: 1 to: 551;
 Translated from: 7 to: 409 (Entire region);
 Genetic Code used: Universal; Wed, Aug 16, 2000 1:40 PM

Frame 1

M	A	Y	G	R	K	K	R	R	Q	R	R	R	M	N				
NAG	ACC	ATG	GCT	TAT	GGC	AGA	AAA	AAA	AGA	AGA	CAG	AGA	AGA	ATG	AAC			
		9			18			27		36			45					
A	L	Q	E	D	T	P	P	G	P	S	T	V	F	R	P	P	T	S
GCG	CTG	CAG	GAA	GAT	ACC	CCG	CCG	GGC	CCG	TCC	ACC	GTG	TTT	CGC	CCG	CCG	ACC	TCC
		60			69			78			87			96			105	
S	R	P	L	E	T	P	H	C	R	E	I	R	I	G	I	A	G	I
TCC	CGC	CCG	CTG	GAA	ACC	CCG	CAT	TGC	CGC	GAA	ATC	CGC	ATC	GGC	ATC	GCG	GGC	ATC
		117			126			135			144			153			162	
T	I	T	L	S	L	C	G	C	A	N	A	R	A	P	T	L	R	S
ACC	ATC	ACC	CTG	TCC	CTG	TGC	GGC	TGC	GCG	AAC	GCG	CGC	GCG	CCG	ACC	CTG	CGC	TCC
		174			183			192			201			210			219	
A	T	A	D	N	S	E	N	T	G	F	K	N	V	P	D	L	R	T
GCG	ACC	GCG	GAT	AAC	TCC	GAA	AAC	ACC	GGC	TTT	AAA	AAC	GTC	CCG	GAT	CTG	CGC	ACC
		231			240			249			258			267			276	
D	Q	P	K	P	P	S	K	K	R	S	C	D	P	S	E	Y	R	V
GAT	CAG	CCG	AAA	CCG	CCG	TCC	AAA	AAA	CGC	TCC	TGC	GAT	CCG	TCC	GAA	TAT	CGC	GTC
		288			297			306			315			324			333	
S	E	L	K	E	S	L	I	T	T	T	P	S	R	P	R	T	A	R
TCC	GAA	CTG	AAA	GAA	TCC	CTG	ATC	ACC	ACC	ACC	CCG	TCC	CGC	CCG	CGC	ACC	GCC	CGC
		345			354			363			372			381			390	
R	C	I	R	L	.													
CGC	TGC	ATC	CGC	CTC	TGA	AAG	CTT	GGC	TGT	TTT	GGC	GGA	TGA	GAG	AAG	ATT	TTC	AGC
		402			411			420			429			438			447	
CTG	ATA	CAG	ATT	AAA	TCA	GAA	CGC	AGA	AGC	GGT	CTG	ATA	AAA	CAG	AAT	TTG	CCT	GGC
		459			468			477			486			495			504	
GGC	AGT	AGC	GCG	GTG	GTC	CCA	CCT	GAC	CCC	ATG	CCG	AAC	TCA	GA				
		516			525			534			543							

FIG. 37

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Frame 1
M A H H H H H Y G R K K R R
NAG ACC ATG GCT CAT CAC CAT CAC CAT TAT GGC CGC AAA AAA CGC CGT
9 18 27 36 45

Q R R R M N A L Q E D T P P G P S T V
CAG CGC CGT CGC ATG AAC GCG CTG CAG GAA GAT ACC CCG CCG GGC CCG TCC ACC GTG
60 69 78 87 96 105

F R P P T S S R P L E T P H C R E I R
TTT CGC CCG CCG ACC TCC TCC CGC CCG CTG GAA ACC CCG CAT TGC CGC GAA ATC CGC
117 126 135 144 153 162

I G I A G I T I T L S L C G C A N A R
ATC GGC ATC GCG GGC ATC ACC ATC ACC CTG TCC CTG TGC GGC TGC GCG AAC GCG CGC
174 183 192 201 210 219

A P T L R S A T A D N S E N T G F K N
GCG CCG ACC CTG CGC TCC GCG ACC GCG GAT AAC TCC GAA AAC ACC GGC TTT AAA AAC
231 240 249 258 267 276

V P D L R T D Q P K P P S K K R S C D
GTC CCG GAT CTG CGC ACC GAT CAG CCG AAA CCG CCG TCC AAA AAA CGC TCC TGC GAT
288 297 306 315 324 333

P S E Y R V S E L K E S L I T T T P S
CCG TCC GAA TAT CGC GTC TCC GAA CTG AAA GAA TCC CTG ATC ACC ACC ACC CCG TCC
345 354 363 372 381 390

R P R T A R R C I R L
CGC CCG CGC ACC GCC CGC CGC TGC ATC CGC CTC TGA AAG CTT GGC TGT TTT
402 411 420 429 438

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FIG. 38

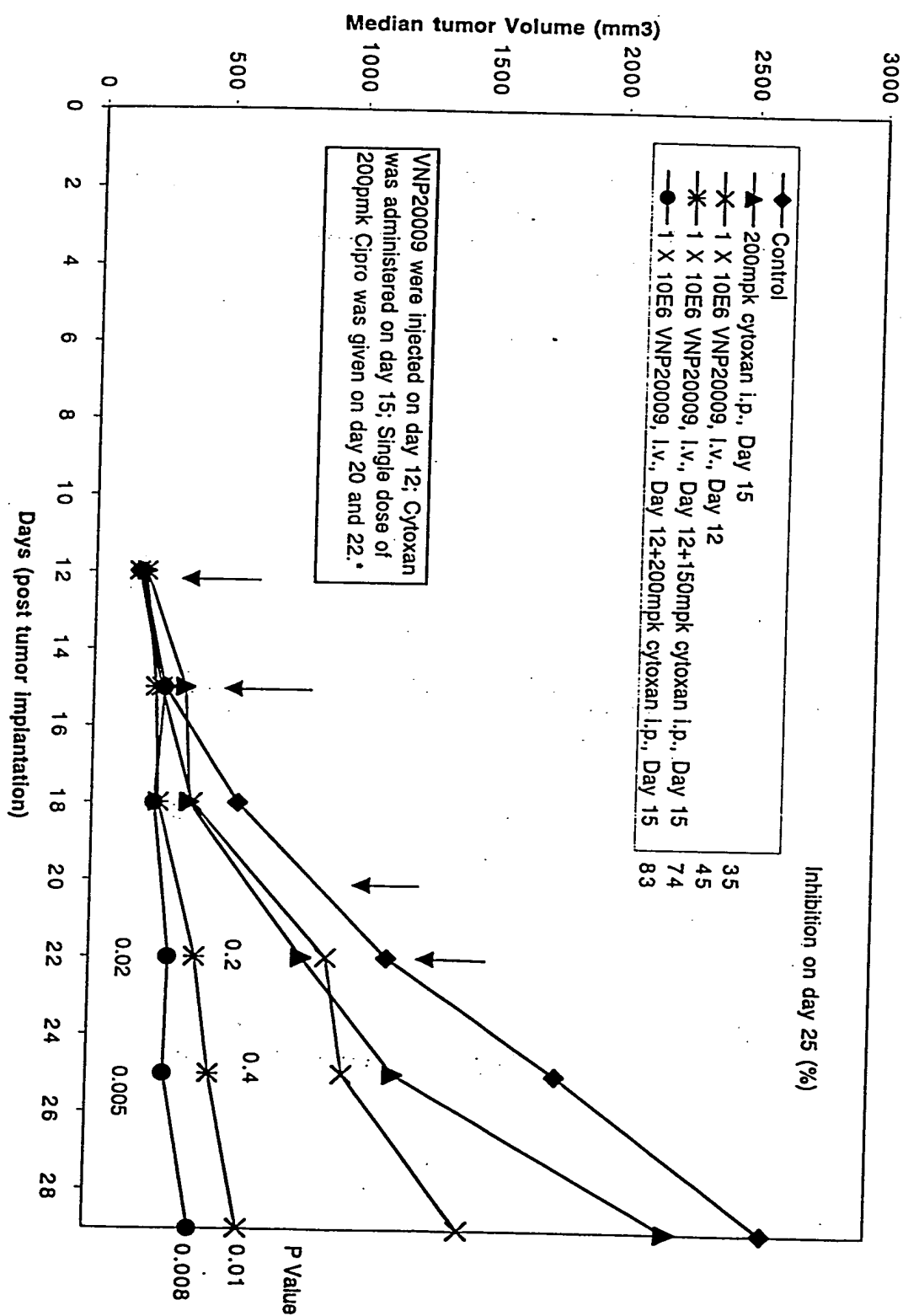


FIG. 39

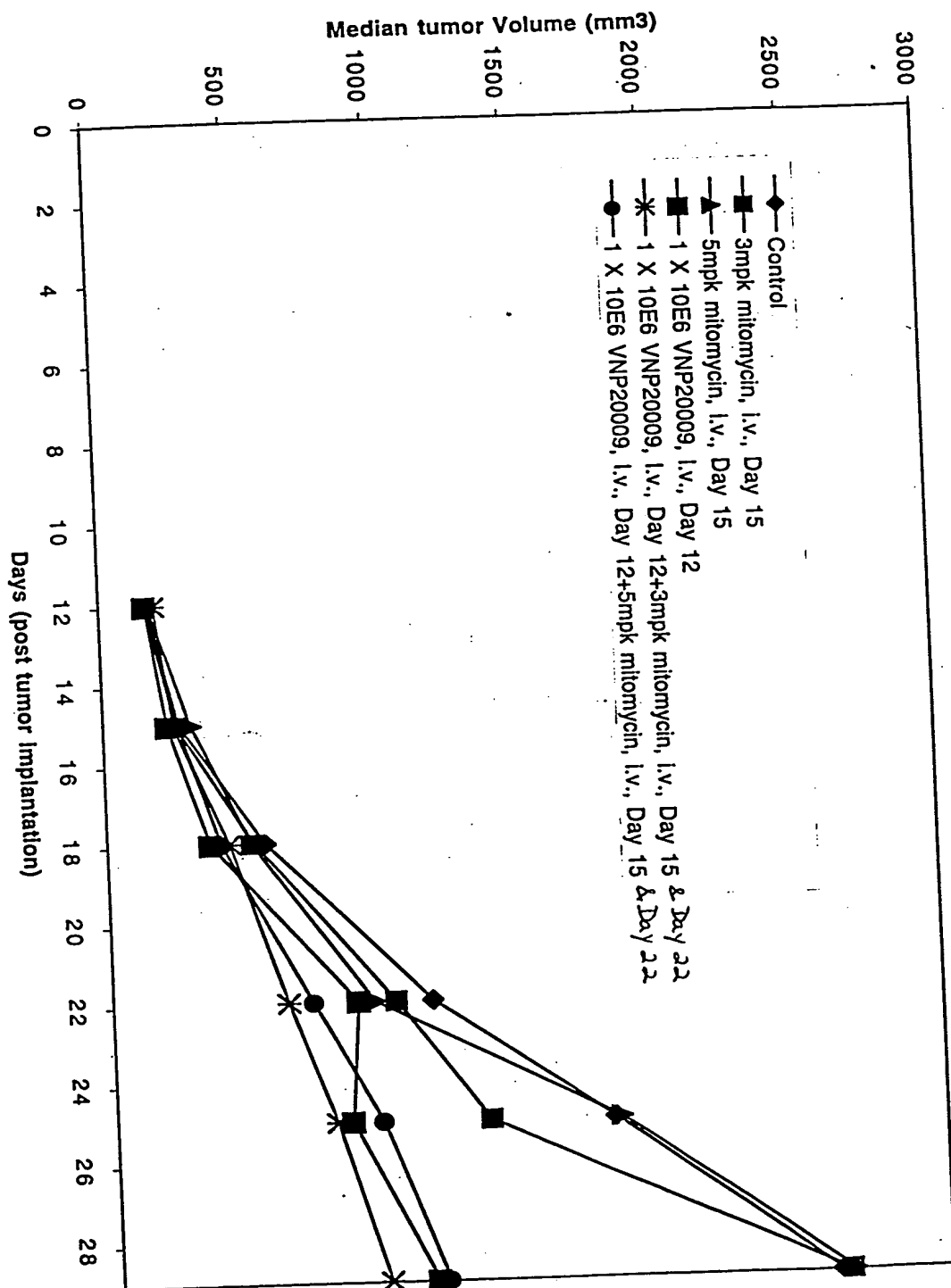


FIG. 40

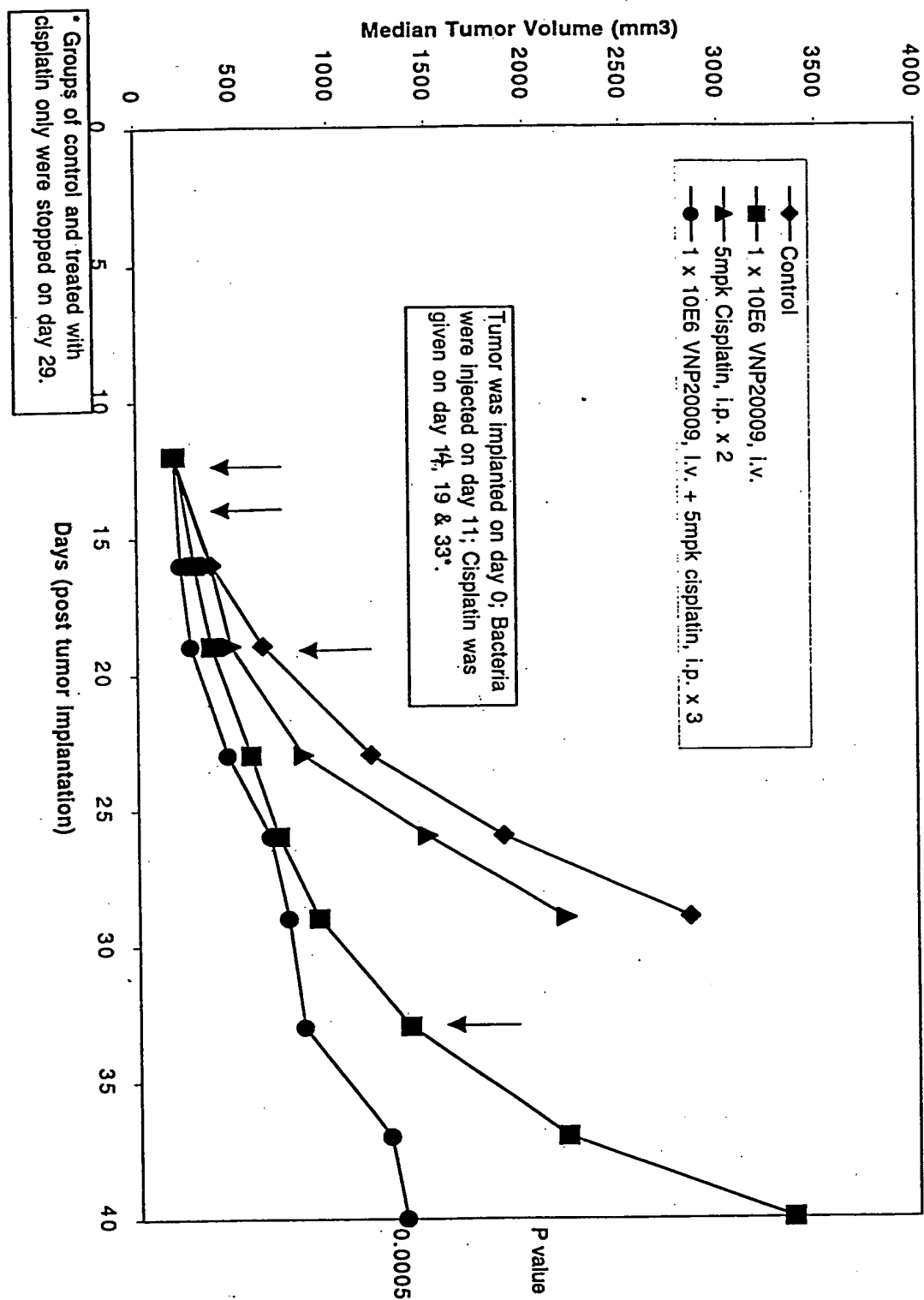


FIG. 41